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OPPORTUNITIES IN PEDIATRIC PRACTICE

CHAIRMAN'S ADDRESS

CLIFFORD SWEET, M.D.

OAKLAND, CALIF.

Pediatrics has much to offer that it did not have twenty-five years ago; but as in all the other specialties in medicine, the number of well qualified practitioners has increased manyfold while all recent graduates, whether in some other specialty or in general practice, have had a far better fundamental pediatric training during their undergraduate days than was available anywhere during the earlier years. Thus, while many more children than formerly are getting adequate pediatric care, there is a much greater number of qualified physicians among whom the patients are divided. If one looks uncritically at the practice carried on by an individual physician, therefore, one may think that pediatric practice is going into an early and perhaps fatal decline and one's mind may turn longingly back toward the "good old days" of the pediatric boom. However, I know of no old days which can be called altogether good when one examines them critically enough to compare all their disadvantages as well as their advantages with those of any given later time, unless a dark age has descended in the meanwhile.

During the earlier years it was easy to become a specialist. A good training in medicine, an interest in a certain field of study, a short time spent familiarizing oneself with whatever knowledge others had accumulated, and the ability to teach oneself from observation soon raised one well above the level of one's confrères. The number of physicians with special training was small, and the number of patients needing special care, much of which could now be given by any competent general practitioner, was great, so all the conditions for "the beaten path to the door" were abundantly present. Also, since in that not far distant day the counsel of the family physician, and even more that of the specialist, was sought only under the pressure of dire need, adequate fees could be charged for emergency care and, once they were paid, years might elapse before there was again any drain on the family purse and no concerted cry against the high cost of medical care was heard in the land.

During my undergraduate years (1905-1912) and for several years afterward there were pediatric teaching centers in this country only at Boston, Chicago and New York (listed alphabetically) and the pioneer work of such teachers as Sedgwick at Minneapolis and Porter at San Francisco, while Howland was just beginning his work at Johns Hopkins. In the other large cities of this country pediatric practice and teaching were carried on by one or two men, and most of them had studied in Berlin or Vienna. This was the eiweissmilch period of American pediatrics.

With few exceptions pediatrics was taught as a minor subject in the departments of obstetrics and medicine. As an undergraduate I attended lectures by the professor of diseases of children, a general practitioner who confined his remarks almost entirely to diseases, usually without clinical demonstration, and a children's clinic held once weekly at which the attendance of as many as five children was remarkable. How greatly this contrasts with the well organized pediatric department, often one of the best teaching divisions, in all the leading medical schools of the present.

While the larger cities were not so nearly saturated with pediatricians and pediatric ideas were not so generally accepted as they now are, most cities of a size that now support several (from three to six) pediatricians were but little affected by pediatric knowledge. Such communities were ideal for the practice of simple or primary pediatrics. The milk supply was dirty, pasteurization was neglected or ineffective, marantic infants were plentiful and many throve on mixtures of boiled skimmed milk, water and sugar, fed at regular intervals, and when death took his toll his visit was not altogether unexpected and "God's will" was accepted. Scorbutus was common, and its prompt cure with orange juice aroused more than passing comment. Rachitis was frequently seen in advanced stages, so that the physician had the courage to prescribe and the patient the hardihood to stomach the cod liver oil then available. The diagnosis of pyuria or of otitis media before rupture of the tympanum and empyema, not to mention lumbar puncture, branded one as a specialist indeed. Infants were fed largely on patent foods procured on the advice of neighbors, relatives and physicians. Fortunately the very limitations of such artificial feeding made insistence on breast feeding easier than it is now.

While sick infants were abundant, one had little or no opportunity to give the preventive care and the guidance which it is now known can play such an important part in the care of well infants and children. I had little or no opportunity for systematic care of well infants during my earlier years of practice except as I extended it as a labor of love and a means of study to those infants whose mothers were under

Read before the Section on Pediatrics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

my obstetric care, in the form of the gratuitous and not always welcome advice which I gave while attending a sick infant or another member of the family or on occasions when the baby was brought to my office to be duly admired and his net weight determined because some question had arisen that could not be answered by weighing him while fully dressed at an obliging neighborhood druggist's or grocer's.

Regularity as a basis for child management was a revolutionary idea, often received by the layman with evident amazement that any one could be so foolish as to suppose that any infant could be taught regular habits, and it was regarded by many physicians as an unnecessarily fussy modern notion. So with few exceptions infants slept with their parents and were nursed, fed, fondled, jigged and carried about as fancy dictated. I have often wondered if the rise of golf as a form of exercise may not have had some relationship to the decline of floor walking with an infant in arms during the night.

In the medical centers at that time pediatric practice, while not so limited, was still hedged about by various complicated forms of infant feeding, and the pediatrician was distinguished from his fellow practitioners largely because he alone possessed the basic training in the care of infants and children which has been taught in more recent years to all graduates in medicine.

From many quarters have come grave doubts concerning the future of pediatrics as a specialty in medicine. While those doubts are a natural outgrowth of the changes which have taken place in the fundamental structure called society, of the even more rapid progress which has been made in medicine, including pediatrics, and of human nature when faced by changing conditions, I think it profitable to consider briefly the advantages and the hopeful signs for the future with which such doubts and fears may be offset. Doubt, fear and distrust of an uncertain future are an inescapable part of the thought of all intelligent creatures. The only defense against becoming hopeless and overwhelmed by fear, doubt and distrust of the future is to stop and give time and thought to the courage, the will to live and be happy, the intelligence and the faith which have carried mankind so far above his original bestial state and which are a priceless part of the heritage of each. A philosophy of reasonable hopefulness must dominate the lives of those who are devoted to planning the very foundations on which children are to erect their lives.

REQUIREMENTS FOR A SPECIALTY

Any division of medical practice which is truly a specialty must fulfil two fundamental qualifications. First, it must have a continuing record of accomplishment which could not be an outgrowth of the general practice of medicine, and, second, it must challenge an appreciable number of the best minds in the medical profession to become proficient in its practice and to make ever greater its service to mankind by the addition of new knowledge and practical applications of that knowledge to the needs of men.

Pediatrics fulfils these fundamental definitions of a specialty. Its record of accomplishment is reflected not only by its large part in the diminished infant and child mortality but in better care for and understanding of children among civilized people everywhere, and above all in the greatly increased ability of all practitioners of medicine in all specialties and in general practice to care for children. In fact, the devoted and unselfish teachers of pediatrics have done their work so well that the very excellence of their teaching has done more than any other one thing to raise doubts concerning the future need for pediatrics as a specialty. And teachers of pediatrics are not alone those who teach and train students, interns, residents and nurses in medical schools and hospitals but every one who practices good pediatrics in the community in which he lives. Any community which has within it a worthy pediatrician becomes a place in which the level of child life rises, because his teaching influences physicians, nurses, dentists, teachers, parents and, not least, the children—for who is so easily quickened to evangelical zeal by new thought as is the child?

That the present level of medical care for children would have risen naturally as a corollary to the general advance of medicine without the labors, research and devotion of the many men and women who have made it their life work is highly improbable. At least it rose sharply in both scope and excellence coincidentally with the birth of pediatrics as a specialty, has continued steadily upward and certainly has not yet arrived at, or anywhere near, the state of perfection beyond which even greater progress is impossible. The problem of fitting specialized medical knowledge and progress to the peculiar needs of the child will always require for its solution persons who give to it their undivided energy and devotion. In the congress devoted to human welfare, whose members are medical specialists, the child must always be ably represented. The future of pediatrics, I am certain, is made secure by the very fact that children have needs which are different from those of adults. The ability best to serve those needs can be attained only through long study and experience by physicians whose principal interest is in children and in whom there resides a peculiar ability, not possessed by every one, which enables them to understand and enter the intimate life of the child, not as an intruder but as a friend.

Another stone which makes secure the foundation is the concern of the pediatrician for the entire life of the child rather than with some part or system which is suspect or out of order temporarily. As in all other human relationships, this advantage carries with it great responsibility and some disadvantages. In a relationship between patient and physician which can be fruitful and grow in influence only if it continues over years there must be real interest, patience and a quality of leadership on the part of the physician that hardly rests on one who successfully performs a temporary, although great, service such as an operation or even obstetric care. Having given much of himself the pediatrician must accept the misunderstanding and ingratitude which are at times his portion with that nobility of the spirit which causes him to search himself for faults rather than accept the ready to hand satisfaction which comes to one who easily places all blame on another.

PREPARATION FOR PRACTICE OF PEDIATRICS

The practice and the problems of pediatrics demand as thorough preparation and offer as many opportunities for study and research as does any specialty in medicine, if not more. The mastery of present pediatric knowledge requires an amount of time, energy and intellectual acuity that compares favorably with the demands of any other specialty. In addition it challenges its followers in certain peculiar ways. Disease

must be detected and studied in its beginnings, when signs and symptoms yield their evidence only to painstaking study, keen observation and sound judgment developed by experience. Here medicine most often yields her choicest gift, prevention. The pediatrician must know as much about all the other branches of medical practice as the internist does; he must know more than those specialists who treat only some parts of the body, and in addition he must become expert in the special knowledge which should govern the application of treatment to children in respect to health, nervous stability and, especially, growth and development.

Growth and development, with all their variations in the individual, have yielded many secrets to intensive study but have many mysteries not yet solved and can never be reduced to the simplicity of an exact mathematical formula. In this field, peculiar to pediatrics though not its exclusive domain, wise, intelligent and constant study will yield marvelous results, although the student will finally have to agree with Robert Louis Stevenson: "Little do ye know your own blessedness; for to travel hopefully is a better thing than to arrive, and the true success is to labor."

Perhaps not the least of the intangibles which the pediatrician must solve arise from the fact that he must gain a large part of his information indirectly through the observations and reports of parents. A nice evaluation of information filtered through the emotions and the often prejudiced, not infrequently poorly articulate, mind of a layman requires experience and long and thoughtful study of the human mind and emotions.

In addition to all other technical training the pediatrician must learn a sound, efficient technic of teaching, the necessity for which is important in the practice of any branch of clinical medicine but most so in pediatrics. He must be able to convince, teach and often inspire the adult members of the family if he hopes to influence effectively the life of his patient, the child.

All in medicine who are worthy of their calling must have an interest in their patients which goes beyond the mere use of technical skill and the material rewards therefor, but the pediatrician must have genuine emotional, I might say spiritual, attachment to children —a concern for their welfare which will always cause him to accept generously as a considerable part of his rewards the consciousness that he has contributed to life at its beginning. True, the practice of pediatrics must yield him a living and the means with which to carry on his work, but if this is his primary interest he might better choose a specialty in which the financial returns per patient are usually greater.

Finally, pediatrics is the only specialty, with the possible exception of geriatrics, which is limited only by the age of the patient cared for. In this distinction lies, I believe, one of its greatest sources of permanence and strength, allowing its followers much latitude of choice in developing their own peculiar abilities and interests and perhaps making it the pioneer on the trail which all specialties will follow during the coming years. By this I mean that the specialist will more nearly approach the relationship to his patients formerly occupied by the general family physician, in that he will have an ever increasing interest in and concern for his patients in all their problems of living, in health and disease. He will then serve them more freely than most now do in the solution of minor problems, and as now within the limits of his specialized technical training, while he guides and counsels them when they have need for the care and skill of experts in other fields.

ADVANCEMENT OF PEDIATRICS

The principal ways in which pediatrics can be advanced above its present high level are the following: First, of course, the pediatrician must maintain all efforts unabated to protect, understand and enrich the entire life of the child in all its phases, physical, mental, emotional and moral. What greater challenge can there be for any one than that he be a contributor to a generation that has been brought up to face life physically efficient, freed as far as may be of unreasonable fears, with fully developed mental powers and trained in those fundamental qualities of character without which no civilization can long endure? Second, the pediatrician must have a training sufficiently broad and comprehensive to enable him to give children more complete care at reasonable cost. This can best be done on an annual fee basis, and I hope soon to present a detailed paper on this method of carrying on pediatric practice, a method which Gengenbach of Denver found to be quite generally followed in the West but used little, if at all, in other parts of this country. One must remember with Zahorsky [1] that people who have young children are usually at the small income period of their lives. Third, good pediatric care must be extended to rural communities, in many of which there is only a beginning. Fourth, the specialty must give its followers such training that those whose interests and qualifications make them valuable primarily as pediatricians may be able to develop especial ability in the application of other specialized fields of medical knowledge and technic to the needs of children. This means of advance should include the sound pediatric training of the numerous followers of other specialties, many of whose patients are children.

All of these demand certain changes in the procedure of many medical schools and of the societies whose members are specialists. Pediatrics and all the other major specialties in medicine have progressed along similar lines. In all a concerted effort has been made to increase the amount and quality of the teaching given to undergraduates, and three or more years of special training is being offered to interns, assistant residents and residents. Therefore, while all recent medical graduates have a much better fundamental understanding of all the specialties than the graduates of former years, and while the younger general practitioners and those in specialties of a general character, such as internal medicine, are qualified to care for many pediatric problems which were formerly neglected or required the care of a pediatrician, there is the disadvantage that modern medical education, with its great emphasis on specialized training, may cause too early and too narrow specialization.

The increasing turn of physicians toward the specialties is due not only to the increased satisfaction which comes from doing better work within a limited field, the greater honor, the emoluments and the chance to live in the city of one's choice, with perhaps a university appointment, but also to the fact that the graduate of recent years can get desirable hospital appointments, with few exceptions, only in the specialties and is not fitted either psychologically or actually to do general practice. All too often as an undergraduate he specializes as much as possible in order to be more certain

1. Zahorsky, John, St. Louis: Personal communication to the author.

of an appointment in the department of his choice. Should he choose and be appointed to a rotating internship he must spend at least half his time in the department where he hopes to be appointed assistant resident and resident. After finishing this long course of postgraduate training he finds it difficult to get a suitable short term appointment in another department. Or if he goes into general practice for a time he usually cannot return to an appointment in another department, because such posts are filled by men who have remained after graduation to go through the regular succession and too often the head of the department fears that the man who has practiced is too advanced to make sufficiently pliable house officer material.

EDUCATION OF THE PEDIATRICIAN

I think that changes should be made in medical education to broaden the training of the specialist and make is easier for the man who is in general practice to get the best training in the specialty of his choice; and by the best training I mean a hospital appointment rather than a postgraduate course. Every reasonable effort should be made to discourage the undergraduate from becoming prematurely a specialist. This can be done by helping him to realize that the best basis for any specialty is the greatest possible attainment in all fields of medical knowledge. Even more can be accomplished by the assurance that his hospital appointment will depend on the excellence of his work, his showing of sound judgment and above all his manifestation of such attributes of character and personality as will make him one of those best fitted to carry on the highest ideals of medicine, rather than on his exclusive attention to and cultivation of a single department and its teaching staff.

During the hospital years capable house officers should be encouraged to spend at least one year working in one or two departments other than the one in which the following two years will be spent. I can think of no better training for pediatrics than a year spent in the surgical, the orthopedic or, perhaps best of all, the ear, nose and throat service. I am certain that at least six months or, better, an entire year in pediatrics would be of great value to the future patients of any specialist who may care for a considerable number of children. Such an exchange of interns should be made a part of a deliberate plan even though it would entail some administrative difficulties and would demand closer attention to the service by the teaching staff for a time after the exchange. It would also make necessary the amendment of the by-laws of some academies and colleges to remove the condition that time must be spent in preparation for the practice of a specialty and to substitute evidence of fitness and accomplishment as the major requirement for admission and certification. This change would be following the recommendation of many leaders in education, who are advocating comprehensive tests of accomplishment without regard to time spent in preparation as the basis for degrees and other honors. Such a program would be of especial and peculiar benefit to the young pediatrician, and automatically it would enable young practitioners to live and work in urban communities, where a too rigid limitation of practice would prevent them from making a decent income.

Opportunity for physicians who have spent a few years in general practice to return to hospital positions rather than to the lesser benefits of formal postgraduate courses is, I believe, greatly to be desired, and a valuable by-product would be the encouragement given to younger graduates to go into general practice for a time and then return for further training.

THE CHALLENGE OF PEDIATRICS

The work of pediatrics has not been completed. It offers an ever increasing challenge, asking its followers to pray not only for more worlds to conquer but for wisdom and energy sufficient to meet the heavy demands placed on them. While the solutions of the older, simpler problems of feeding and regulation of the life of the infant have become fairly common knowledge and are reasonably well practiced, there remain many more numerous and complex problems.

Family life no longer rests on the simple predicates of a father who was the lord and master of the household; a mother who was the family drudge, in whom it was unseemly to complain openly of her lot, even though loss of temper, with satisfaction (the "release" of modern psychiatry) obtained from dealing out swift and summary punishment, caused no criticism or upbraidings of conscience, and children who were "seen but not heard" but were under the constant and beneficent discipline imposed on them by their share in the necessary tasks of everyday family life. The empty water bucket and wood box were powerful disciplinary forces, for which it is difficult to find counterparts in modern life. Pediatricians can do much for parents and children as teachers and interpreters of modern knowledge, not only to make smooth the ways of family life but to make it, as it must always be, the greatest means of fitting the child for the abundant life. He can help the father back into his rightful place in the family circle, from which modern economic life has almost removed him, and he can lead the distracted mother out of the mire of partially understood child psychology, in which she wanders in constant fright of Giant Malnutrition and of Giant Despair, lest some slight fault of hers may hurl her child into the eternal abyss where conditioned reflexes and repressions have their abode.

The new field of the adolescent period (from 12 to 18 or even 20 years) is best approached by the pediatric route. Sound training of parents and children throughout the preadolescent years will reduce the difficulties of this period to a minimum, and the pediatrician who gives of himself to the care of children from babyhood onward literally grows into an understanding of these problems and a sympathy for the "big children" which can be gained in no other way.

A sound working knowledge of endocrinology must have a considerable place in pediatric practice. With due respect to the limitations of the present state of knowledge and its practical applications to growth and development, I feel that this field of therapy may well usher in a new era of human welfare.

Pediatric training is an excellent foundation for the study of any branch of medical knowledge which may be the lifelong interest of the student. For example, surgery has its special applications during childhood, while the study of body mechanics during normal growth and development in individual patients will add much to the clarification and practical application of this very important branch of child welfare. Allergic hypersensitiveness is sufficiently different in its manifestations during childhood and during adult life to justify the giving by some of its students of especial attention to the problems peculiar to the earlier years of life. Or one's interest and abilities may lead one

to study the central nervous system intensively. Such a study will not only be absorbingly interesting but will be most valuable if practice is carried on in communities which are not well supplied with neurologic skill and knowledge. A knowledge of the ear, nose and throat will enable the pediatrician to treat infections of the respiratory tract at least as well as and I think better than any other practitioner. The contagious diseases, with their complications, will yield results in both curative and preventive medicine to any one who plows deeply in this field instead of merely harrowing, as is still too often done. The pediatrician is especially fitted to deal with the public health aspects of medical care for children. This activity will be of especial importance in rural communities, where, as I have said before, good pediatric care is badly needed; but there is a great need for pediatric guidance in the larger centers also.

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THE TREATMENT OF ADDISON'S DISEASE

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Time will not allow detailed discussion of the historical background, etiology or pathology of Addison's disease. This can be found in the monograph by Rowntree and Snell.[1] This paper will therefore be limited to a consideration of the essential points of treatment.

Briefly the principles behind the management of patients with Addison's disease are as follows: In the first place, these patients are suffering from a destruction of the adrenal cortex. Earlier reports, such as that by Barker,[2] showed a high incidence of tuberculous destruction. Recent reports reveal an increasing incidence of simple atrophy of the cortex, but it will require more time to determine whether this change in incidence is more apparent than real. Guttman[3] found that the duration of the disease was longer when primary atrophy of the cortex was present (34.02 ± 4.40 months) than when the cortex was destroyed by tuberculosis (13.15 ± 2.54 months). If there is tuberculous destruction of the adrenal cortex, then, in a high percentage of cases, tuberculosis is present in other parts of the body. It sometimes happens that the attending physician can effectively correct the deficiencies caused by Addison's disease and yet the patient dies of renal, osseous, pulmonary or peritoneal tuberculosis. If the patient with Addison's disease does have tuberculosis, he must receive special care for this condition. If the patient has active pulmonary tuberculosis, the prognosis is very bad.

In the second place, regardless of the cause of the destruction of the cortex, there follows a lack of adrenal cortical hormone or hormones. Detailed biochemical and physiologic studies of these substances may be found in the published reports of Hartman,[4] Kendall,[5] Grollman,[6] Zwemer[7] and Swingle.[8] Here only the fact need be mentioned that the cortical hormone or hormones are essential to life and that they have at least one important function, the control of the blood electrolytes. I will not discuss other functions except to say that there is evidence to suggest that the adrenal cortex plays a prominent role in carbohydrate metabolism.

Thirdly, since patients with Addison's disease lack this cortical hormone, they show changes in the blood electrolytes, namely a loss of chloride and sodium from the body with a retention of potassium, an increase in urea, a marked loss of fluids (with resultant hemoconcentration) and sometimes a marked hypoglycemia. These changes are incompletely understood.

Efforts to correct the disturbances of Addison's disease have proceeded along three lines: The first type of treatment consists in the addition of sodium, in the form of sodium chloride, and either sodium citrate or sodium bicarbonate. Loeb[9] deserves great credit for his emphasis on the importance of administering large amounts of salt. The second type of treatment consists in the restriction of potassium in the diet; this is described in detail in an article by Wilder, Kendall, Snell and their associates.[10] A third type consists of treatment with an active extract of the adrenal cortex.

Treatment by these three methods or by a combination of them has aroused much controversy. Some believe that all patients with Addison's disease can be treated successfully by the use of sodium salts alone and that the use of a low potassium diet and cortical hormone is not necessary. Others believe that if patients receive enough hormone they need pay little attention to their diet and do not need to take large amounts of sodium salts.

Thompson[11] has made some interesting observations. He says:

> We have followed three patients with marked Addison's disease, on a normal diet and with no other form of therapy except 10 to 20 cc. daily of Wilson's adrenal cortex extract, for a period of several months to over two years. This, of course, was after they had been brought out of crisis by other additional treatment. With the extract alone, it has been possible to get them to gain large amounts of weight and in general to carry on their normal activity, provided no active tuberculous infection is present. Although some reduction in pigmentation has occurred, it has not disappeared completely, leading us to believe that the extract, at least in the doses we have administered, does not represent complete replacement therapy.

The present paper is not given in the hope of settling this controversy but rather for the purpose of reviewing what may be considered to be adequate methods of therapy. I shall discuss the treatment of Addison's disease by means of the presentation of hypothetic case

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From the Division of Medicine, the Mayo Clinic.

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This paper does not represent the opinions of any single individual. It represents the composite experience of the members of the Sections on Biochemistry and Clinical Medicine of the Mayo Clinic.

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11. Thompson, W. O.: Personal communication to the author.

histories recorded, for purposes of emphasis, in an informal manner. For the sake of uniformity I will assume that all the patients are men. Actually, of course, the disease more frequently affects women (1.6 to 1).

THE PATIENT IN A CRISIS OF ADDISON'S DISEASE

A patient is admitted to the hospital on a hot afternoon in July in a crisis of Addison's disease. He is too ill to be bothered with an exhaustive quizzing and is put to bed. The room is made as quiet and restful as possible. Any conversation regarding his case is carried on outside the room, for there is no illness more acute than this. During a brief wait for the necessary supplies for treatment the patient's wife, we'll say, tells the essential points of the history. Her husband had been well until three months previously, when he began to complain of loss of weight and strength. His appetite had "fallen off" and he had developed a real "craving" for salt. There had been some nausea and troublesome spells of hiccuping. She had noticed that his skin had changed in color; it was darker, and yes, come to think of it, she had noticed the appearance of many freckles which looked like india ink. In the last few days "since it got so hot" he had become much weaker and hadn't been able to go to work. Today he had vomited everything she had given him and had had a troublesome diarrhea. He had then complained of severe epigastric pains and finally had "just collapsed" and they had brought him to the hospital.

TABLE 1.—*The Blood in the Crisis of Addison's Disease (Hypothetic Case)*

	Mg. per 100 Cc.				
	Normal Values	First Day	Second Day	Third Day	Tenth Day
Urea	10-40	120	80	60	40
Chlorides	570-620	440	480	520	590
Sodium	315-330	260	270	290	320
Potassium	16-22	26	24	23	20

The physician returns to the room. He examines the patient to determine two things: how low his blood pressure is and how dehydrated he is. The physician does not test the eye reflexes, he does not attempt to palpate the liver, kidneys and spleen, and he does not make a rectal examination. Furthermore he sees to it that the nurses forget the routine for admitting new patients; there is no bath, no rolling the patient around, no enthusiastic administration of an enema (patients suffering from Addison's disease also are made worse by purging). The attending nurses therefore enter into the conspiracy for kindly quiet.

The treatment tray has now arrived. It contains supplies for the collection of specimens of blood and for the intravenous administration of fluids. A needle is placed in the vein and enough blood is withdrawn for the determination of its content of sugar, urea and chloride. Blood may also be taken for analysis of sodium and potassium, although this is not urgent. Without withdrawal of the needle, the administration of a solution composed of 10 per cent dextrose, 1 per cent sodium chloride and 0.5 per cent sodium citrate is begun. To the solution is added 30 cc. of adrenal cortex extract. The patient is made comfortable and quiet again reigns.

But let us say that it is Sunday afternoon and the laboratory technician can't be reached immediately. It makes little difference. There is probably no other condition in which examination of the patient and his blood is so unimportant and in which prompt and energetic treatment is so all important. Regardless of what the laboratory tests show, immediate treatment is the same. The reason for ascertaining the sugar content of the blood is that sometimes there is an acute hypoglycemia and large amounts of sugar are urgently needed. Dextrose should always be accompanied by salt. Allers, Nilson and Kendall [12] have shown that when dextrose alone is injected into adrenalectomized animals the initial hyperglycemia may be followed by a fatal hypoglycemia. The determination of the amount of urea and chlorides in the blood gives the physician a basis for judging subsequent improvement and guiding subsequent treatment. There are tests other than those of the sugar, urea and chloride content which are of considerable interest to students of this disease. Such tests are for blood volume and the amount of sodium and potassium in the blood. These tests, however, are beyond the reach of many physicians and laboratories. The patient I am now considering is found to have the usual changes in the chemical constituents of the blood (table 1).

Within an hour or so the patient is then found to have improved. His blood pressure has risen from 70 systolic and 50 diastolic to 86 systolic and 60 diastolic (the blood pressure often rises slowly and may never reach normal). The epigastric pains are less and he is much more responsive. He asks for a drink and is given fluids ad libitum. The intravenous administration of fluid is continued during the night and another 20 cc. of adrenal cortex extract is added to the solution. By morning he may have received 3 or 4 liters of this solution and 50 cc. of the extract. The value for blood urea has dropped to 80 mg. per hundred cubic centimeters and the plasma chlorides have risen to 480 mg. The patient is feeling infinitely better and the needle is taken from his vein. Now he may be bathed and given general nursing care, but only those things necessary for his comfort are allowed. He is now given "Addison's elixir" [13] to drink.

In the afternoon the patient again feels weak and 2,000 cc. of the solution is again given intravenously together with 20 cc. of adrenal cortex extract. No one can foretell how long it will be necessary to keep up this "emergency treatment." (Snell and Morlock [14] reported one case in which 255 cc. of adrenal cortex extract was required in nine days, during which time the patient received more than 20 liters of fluid intravenously; at the end of this period recovery from the crisis was complete.) In a few days the patient feels much improved and treatment is instituted which is similar to that to be described for the patient with chronic Addison's disease.

No single case, of course, can illustrate all the features of Addison's disease. For example, the crisis did not occur in this case until the patient had had symptoms for several months. In some cases a patient's crisis may be the first indication of his illness. Furthermore, while this patient's crisis responded rapidly to treatment, another patient might have been seriously ill for

12. Allers, W. D.; Nilson, N. W., and Kendall, E. C.: Studies on Adrenalectomized Dogs: The Toxic Action of Potassium, Proc. Staff Meet., Mayo Clin. **11**: 283-288 (April 29) 1936.

13. To 1 liter of water 10 Gm. of salt and 5 Gm. of sodium citrate are added. This is flavored to taste with fruit-flavoring extracts (such as those of the Calumet Tea and Coffee Company, Chicago) and is kept well iced. The patient should drink at least 1 liter of this each day.

14. Snell, A. M., and Morlock, C. G.: Neurologic Symptoms Produced by Suprarenal Insufficiency: Report of a Case, Proc. Staff Meet., Mayo Clin. **11**: 551-554 (Aug. 26) 1936.

a week or more. On the other hand, the patient's symptoms may be quite different from those recorded in this case. In this case the gastrointestinal symptoms were prominent. In Snell and Morlock's case, which has been previously referred to, there were so many symptoms related to the nervous system that an associated tuberculous meningitis was suspected. In still other cases the patient's symptoms may be largely associated with circulatory collapse. Each case is therefore different and requires individualized treatment.

Many deaths from the crisis of Addison's disease are due to delayed recognition of the condition or to a delay in treatment. Treatment must be both prompt and energetic. The importance of administering large amounts of sodium chloride cannot be overemphasized. During the crisis some patients may lose as much as 10 pounds (4.5 Kg.) in two days; this loss of weight is largely a loss of fluid, and fluids and sodium salts must be replaced.

THE PATIENT WITH ADDISON'S DISEASE WHO REQUIRES AN OPERATION

Surgery of even the simplest type was until recently denied patients suffering from Addison's disease. The extraction of a tooth was formerly sufficient to cause death. Fortunately this state of affairs no longer exists, and it is now possible to perform necessary operations, although, of course, there is an increased risk.

Briefly, let us say that this patient presents the typical appearance of Addison's disease but in addition is suffering from tuberculous destruction of the left kidney. It is considered advisable to remove this kidney. The patient knows that without this operation his outlook is very dark and he agrees to accept the chance which operation offers. The preoperative preparation requires at least a week and consists in placing him on a regimen which includes the low potassium diet (to be described later), the daily oral administration of a quart of "Addison's elixir" and the daily intramuscular or subcutaneous injection of 10 cc. of adrenal cortex extract. On the morning of the operation the patient receives by intravenous injection 2 liters of a solution of 10 per cent dextrose, 1 per cent salt and 0.5 per cent sodium citrate with 20 cc. of the extract. This procedure is repeated after the operation. The length of time that intravenous treatment and careful observation are necessary depends on the patient's condition and it may vary from several days to several weeks. On this regimen the patient makes a very satisfactory recovery. He owes his life to the close cooperation between surgeon and physician and to the energetic application of the measures just mentioned. Precision is demanded; there must be nothing slipshod in the treatment of such a patient as this.

Many patients who require operation for the destructive lesions of chronic tuberculosis suffer from a postoperative reaction which may be described as a "severe tuberculin reaction." This does not occur more frequently among patients suffering from Addison's disease, but it is more dangerous in association with this disease. The accompanying chart (of an actual case) demonstrates both the severe reaction, the temperature going to 105 F., and the energetic treatment which was required for more than two weeks' time.

Patients with Addison's disease are also extremely sensitive to certain types of medication. A very small amount of insulin or thyroid extract may kill a patient with Addison's disease.

THE PATIENT WITH CHRONIC ADDISON'S DISEASE

This patient's skin is typically pigmented and he has experienced some of the other symptoms of the first patient who was admitted in crisis, but in a milder form. This is his third admission, and he enters the hospital under his own power.

He was first seen, we will say, in the spring of 1935, when the diagnosis of Addison's disease was made. He did not have a particularly severe form of the disease and it was not believed necessary to administer adrenal cortex extract. Ten Gm. of salt and 5 Gm. of sodium citrate were prescribed, to be taken daily by mouth. This was first given in the form of enteric-coated tablets, but when the patient did not improve, his stools were passed through a sieve and the tablets were recovered unchanged. This amount of salt and sodium citrate nauseated him when swallowed in capsules. "Addison's elixir" proved very satisfactory. Examination of the patient's lungs disclosed the presence of pulmonary tuberculosis, but there was no evidence of activity.

The patient's second admission was during the summer of 1937. He had enjoyed improved health since his first admission. When a bad cold developed he had become quite weak, but he had drunk 2 quarts

Addison's disease and chronic tuberculosis, showing severe postoperative reaction.

of the "Addison's elixir" each day instead of one and had made a rapid recovery. The reason he gave for returning at this time was "this hot weather has got me down and the salt won't pull me up."

Since the time of this patient's first admission it had been observed that potassium is very toxic to patients with Addison's disease. It was believed that the reason for the patient's continued difficulty was the fact that his food contained too much potassium. Sister Victor [15] was therefore asked to plan a diet which contained only small amounts of potassium. The suggestions and diet were as follows:

A PLAN FOR A DIET LOW IN CONTENT OF POTASSIUM

In arranging a diet restricted in potassium, it is necessary (1) to limit the selection of bread, cereal and sugars to the highly refined products, (2) to restrict moderately the use of milk, meat, fruits, vegetables, condiments and certain beverages, and (3) pending further investigation to cook meat and vegetables according to a special method whereby the content of potassium is reduced.

The special method suggested for the cooking of vegetables consists in cutting the vegetable into small pieces and cooking them in from six to eight times as much water as vegetable. Cooked according to this

15. Victor, Sister Mary: Diets Low in Content of Potassium (unpublished data).

method, the potassium is reduced from 60 to 70 per cent without a concurrent diminution of palatability. The special method suggested for the cooking of meat consists in cutting the meat into small pieces and cooking it in a so-called parchment paper bag in from six to eight times as much water as meat. By this method the content of potassium is reduced to a fourth of the original level while other nutrients and extractives which give flavor are retained in the meat.

Foods to be strictly avoided because of their high content of potassium include soups, broths and gravies containing meat stock or meat extracts, catsup, chili sauce, mustard and other meat sauces and seasonings, dried fruit and vegetables, bran, molasses, Postum and chocolate.

A plan for an adequate diet in which the content of potassium does not exceed 2 Gm. is given in table 2.

TABLE 2.—*Adequate Diet in Which Potassium Does Not Exceed 2 Gm.*

	Gm.	Approximate Measure
For breakfast:		
Orange or grapefruit	100	1 average-sized serving
Cream of wheat	15	1 average-sized serving
Egg	50	1
Bacon	10	2 small strips
Bread, white (may be toasted)	30	1 slice
Butter	10	1 square
Cream	90	½ cupful (scant)
For second meal:		
Meat, specially cooked	75	1 fairly large serving
Potato, specially cooked	100	1 serving
Raw vegetable (lettuce, celery, tomato, cabbage, Swiss chard or watercress)	100	1 serving
Mayonnaise	15	1 tablespoonful
Bread, white	30	1 slice
Butter	20	2 squares
Fruit (apples, pears, strawberries or tangerines)	100	1 serving
Cream	30	2 tablespoonfuls
Milk	200	1 glass
Cheese	20	1 cubic inch
For third meal:		
Egg	50	1
Polished rice (weighed dry)	25	1 serving (½ cup)
Vegetable (specially cooked asparagus, carrots, onions, turnips or squash)	100	1 serving
Bread, white	30	1 slice
Butter	20	2 squares
Fruit (apples, pears, strawberries or tangerines)	100	1 serving
Cream	30	2 tablespoonfuls
Milk	100	½ glass

Further details regarding this diet will be found in an article to be published by Sister Victor.

Lists of permitted substitutions and more detailed directions for the special cooking of meat and vegetables are given in a paper to be published in the *Journal of the American Dietetic Association.*

All foods should be weighed or carefully measured. One cup of weak coffee and two cups of weak tea are allowed daily. Salt may be used in generous amounts, particularly in seasoning the specially cooked foods. Pepper and vinegar are allowed in moderation. White sugar may be used liberally in beverages, on cereal and on fruits. Gelatin, either plain or flavored, may be used in salads or desserts. Carbonated beverages, such as ginger ale and coca-cola, as well as fruits prepared from synthetic beverage powders or crystals, may also be taken as desired. Any one of these beverages may be used as a carrier for the "extra" salt usually prescribed.

By using this plan as a basis and by making appropriate substitutions for the foods listed, many varied and attractive menus can be planned.

The patient improved rapidly and was dismissed, with the advice to follow the "low potassium diet" and to continue to take at least 1 quart of "Addison's elixir" each day; this was to be taken during periods of stress such as are caused by hot weather and intercurrent infections.

On his third admission (say in May 1938) the patient reports that he has been much stronger since he has followed the regimen of "salt, citrate and low potassium diet" than when he simply took salt and citrate and ate a general diet. However, he says that he has not felt well lately and that he has returned for any additional suggestions for improving his health.

The only additional suggestion which can be given at this time is that he should be given adrenal cortex extract. This is likely to be more necessary when pulmonary tuberculosis is present. How much the patient should take will have to be determined by clinical trial in much the same manner as one determines the dosage of insulin for a diabetic patient.

The patient is found to respond satisfactorily to the subcutaneous or intramuscular injection of 5 cc. of extract every day. He is taught the technic of self administration, and by adding 0.5 cc. of 1 per cent procaine to the solution he suffers no discomfort. It may be possible for him to omit the injections on occasions, as, for instance, during the cooler months; it may also be necessary to increase the amount on other occasions, particularly during hot weather and in other periods of stress.

In discussing this case it may be said that the patient's first period of treatment with salt and sodium citrate alone was good; that the second period of his treatment with the valuable addition to the first regimen of a low potassium diet was better; that for this patient the addition of adrenal cortex extract to his previous regimen was additionally beneficial, and constituted, for this particular patient, the best treatment. There have been few patients who have not reported better health when, in addition to controlling the potassium content of the diet and securing adequate chloride and sodium, some adrenal cortex extract was taken. This applies especially to patients who have systemic tuberculosis.

THE PATIENT SUSPECTED OF HAVING ADDISON'S DISEASE

Patients may be suspected of having Addison's disease because of unusual pigmentation, hypotension or weakness—or be just "suspected" of having it. The patient I shall consider now is 18 years old. He is deeply pigmented, but he has just spent the summer as a counselor at a boys' camp and is so sunburned that his color is of no significance; he does not have any "india ink" freckles. He has entered the hospital because he felt quite weak toward the close of the camp period; the camp physician found his blood pressure to be low and the question of Addison's disease was raised. A period of two weeks has elapsed and he is already feeling much improved; however, his parents want the diagnosis proved or disproved. Nothing is found on physical examination or on study of the blood electrolytes to substantiate the diagnosis of Addison's disease. However, it is well known that this is not conclusive, and it is decided to carry out a "provocative test."

Provocative tests should be performed only in the hospital and only when facilities are adequate for immediate treatment if the patient does have Addison's disease and a crisis is induced by the test. Earlier tests, such as the one originally suggested by Harrop and his

co-workers,[16] had as their basis the fact that if Addison's disease was present the patient would be made worse by the withdrawal of salt from the diet and there would be positive changes in the blood electrolytes. However, some patients with unquestioned Addison's disease were found to withstand withdrawal of salt for appreciable periods. In later tests potassium was added to the diet; this accelerated the response if Addison's disease was present and greatly increased the reliability of the procedure. All these tests, however, required that the patient be made worse if the test was to be considered positive—and sometimes the patients were made very much worse. The risk of such a test, therefore, was not insignificant.

The patient I am considering is given the test outlined by Cutler, Power and Wilder[17] and this test will not be described in detail here. It has as its basis the determination of the concentration of chloride in the urine at the end of a brief (fifty-two hour) period of a standard "high potassium-low salt" regimen. This test is the simplest and, in experienced hands, the safest yet described. The results indicate that the patient does not have Addison's disease. He is therefore told that there is no evidence for the diagnosis of Addison's disease. He is also told that, while the test has given every indication of being very reliable, no test is 100 per cent accurate. He is dismissed with the reassurance that his symptoms probably were the result of overwork beneath a hot sun, with an insufficient intake of salt. We insist, however, that he cooperate with his local physician for future observation.

RESULTS OF TREATMENT

It is difficult to evaluate the results of treatment of Addison's disease. There are at least three factors which militate against acceptance of "survival time" as a criterion for conclusions: (1) Some patients have survived for years without treatment of any kind, one patient in a case reported by Snell[18] having lived for seventeen years without the advantage of "modern" treatment; (2) "modern" treatment has been available for clinical trial for an insufficient period of time, and (3) there are too many "variables," such as the different types of extract used and the varying degrees of cooperation between physicians and patients, to permit statistical comparison of different groups of cases as treated in different parts of the country.

Greene[19] appreciated these difficulties in collecting material for his recent excellent and thorough study, in which he reviewed his personal experience in thirty-four cases of Addison's disease. This had begun when he and Rowntree, with Snell, were studying these cases at the Mayo Clinic. Greene compared this group of thirty-four treated patients with 266 untreated ones and concluded: "The treatment added little to the apparent life expectancy in many cases but definitely prolonged life in a limited group of cases. The duration of the disease was more prolonged in this series of cases than has been reported with earlier methods of treatment."

Hausner, Snell and I[20] have recently compared the results of treatment in two groups of cases seen at the clinic. The first group of forty-six patients was seen between May 1, 1930, and Oct. 1, 1933. Adrenal cortex extract was introduced at the beginning of this period and treatment with sodium chloride in the middle of it. The second group, of forty-three patients, was seen between Oct. 1, 1933, and July 1, 1937. The use of sodium bicarbonate or sodium citrate was introduced early in this period and after May 1935 the low potassium diet was used. These two groups are more suitable for comparison than would be true of patients treated in different localities. The deaths at the end of the period that ended Oct. 1, 1933, numbered thirty (65 per cent); the deaths at the end of the period that ended July 1, 1937, numbered seventeen (40 per cent).

Of the seventeen patients in the second series who died, six were women, not one of whom was given the low potassium diet. Of the eleven men who died, only four were given what might now be termed "adequate" treatment. Perhaps a better idea of the efficacy of the newer type of treatment can be obtained from the knowledge that from Oct. 1, 1933, to Oct. 1, 1934, eight deaths occurred in seventeen admissions, whereas from July 1, 1936, to July 1, 1937, there were only three deaths in fourteen admissions, two of them in cases in which extensive tuberculosis had caused marked destruction of the vertebrae. Thus from a very brief analysis of these crude mortality statistics it is seen that definite improvement has followed the application of what might be termed the "latest" type of treatment.

Far more important than this type of analysis, however, is the knowledge which has been gained from observations that do not lend themselves to statistical study. By this I refer to the fact that all of us who have been treating Addison's disease for many years have noticed that, with our present method of treatment, most of our patients are feeling better than they ever did with previous types of treatment. Many are able to follow gainful occupations and to resume their place in society. One of our patients, a young woman who was rescued from a crisis which in former years would have resulted in her death, is now teaching school every day and is feeling quite well. Another young man is working every day and is the proud father of a son, the first patient with Addison's disease, of whom we have knowledge, who has become a father. We have no record of a woman with Addison's disease having had a child, but Kendall[12] has reported the successful delivery of healthy pups in the case of an adrenalectomized dog that had been maintained with sodium chloride and sodium citrate without adrenal cortex extract for months before and during gestation. Furthermore, patients with Addison's disease can, with this treatment, survive stresses which formerly would have caused their death. They no longer die in large numbers during the first hot spell of the summer. They now are able to have necessary surgical operations and can withstand minor intercurrent infections.

Patients with Addison's disease will continue to die from tuberculosis; until we learn more, others will die from causes which we do not understand. These deaths are unfortunate, of course, and serve as a challenge for future study. But there are many other deaths which

16. Harrop, G. A.; Weinstein, Albert; Soffer, L. J., and Trescher, J. H.: The Diagnosis and Treatment of Addison's Disease, J. A. M. A. **100:** 1850-1855 (June 10) 1933.

17. Cutler, H. H.; Power, M. H., and Wilder, R. M.: Concentrations of Chloride, Sodium and Potassium in Urine and Blood: Their Diagnostic Significance in Adrenal Insufficiency, J. A. M. A. **111:** 117-122 (July 9) 1938.

18. Snell, A. M.: Addison's Disease of Unusually Long Duration, Proc. Staff Meet., Mayo Clin. **9:** 303-307 (May 23) 1934.

19. Greene, C. H.: Clinical Use of Extract of the Adrenal Cortex: Report on Thirty-Four Cases of Addison's Disease Studied Between 1930 and 1937, with a Review of the Literature, Arch. Int. Med. **59:** 759-784 (May) 1937.

20. Rynearson, E. H.; Snell, A. M., and Hausner, Erich: Behandlung der Addisonschen Krankheit und ihre Erfolge, Ztschr. f. klin. Med. **134:** 11-30 (April 14) 1938.

are most regrettable because they could have been prevented if only knowledge which is already available had been utilized. Many of these deaths are due to negligence on the part of the patient. The patient must be taught that his safety depends on being just as vigilant as any patient with severe diabetes, or more so; he must follow his diet as closely, in order to avoid a dangerous intake of potassium, and take his sodium salts and extract just as religiously as the diabetic patient follows his diet and takes his insulin. He must avoid stresses and strains such as intercurrent infections and hot weather even more carefully and he must cooperate with his physician most faithfully.

Other deaths which could be prevented are those which follow the delayed recognition or incomplete treatment of an acute crisis. Again this emergency can be compared to the emergency of diabetic coma. The patient with Addison's disease must learn the warning signs of impending trouble and he must hasten to his physician, who must be prepared to treat him promptly and energetically. Not all patients in the crisis of Addison's disease can be saved, but most of them can.

Finally it should be stated, as mentioned previously, that there are some patients with Addison's disease who die in spite of energetic treatment, which includes all the suggestions mentioned here. They die in spite of the fact that chemical analysis of the blood indicates the return to normal values of the electrolytes. We do not know why they die. This is but one of the many unsolved problems concerned with Addison's disease.

No attempt has been made in this paper to create the impression that a cure for Addison's disease is being announced. Far from it. Progress is being reported, however, and it is believed that the best available treatment should consist in (1) the restriction of potassium in the diet, (2) the addition of sodium salts to the diet, (3) the use of an active extract of the adrenal cortex when it is needed, (4) the training of the physician and the patient in the details of treatment of the chronic state of the disease, and (5) the early recognition of acute remissions and their energetic treatment.

ABSTRACT OF DISCUSSION

DR. HERBERT M. EVANS, Berkeley, Calif.: Dr. Rynearson's report is particularly valuable to the profession because the malady is so rare that only a clinic like that at Rochester would have the opportunity of treating any considerable number of cases. It was at that clinic that the first conclusive evidence of the value of substitution therapy in the classic efforts of Rowntree and Snell with the extracts of a decade ago was shown. In addition to the advances as to the group of substances which may be designated as adrenal cortex principles, in which Kendall has had a significant part, equal attention has been paid the newer knowledge of the sodium-potassium metabolism in these patients. Recently, by the use of a new tool, Dr. Anderson of our laboratory, in conjunction with Lawrence, has confirmed the observations of Loeb, Harrop and others that adrenal subnormality involves the increased secretion of sodium and retention of potassium, the new tool being the use of tagged atoms of sodium potassium, those on which radioactive properties have been imposed by the cyclotron. In conditions of subnormality or destruction of the adrenal cortex, it is natural to look for subnormality in each of the known functions of the adrenal cortex. But for the present one can, perhaps, dismiss the capacity of this tissue to secrete estrogens and androgens or some substances related to the sterols of the sex hormone group. There appears to be no question that the primary object of concern here is the adrenal secretion of the vitally necessary substance which regulates the metabolism of the electrolytes. From the recent studies of Long and others it is known that the same hormone plays an important role in the metabolism of carbohydrates. One of the most debated questions is whether the mediation of the pituitary in carbohydrate metabolism is to be explained solely by its control of this function of the adrenal cortex. That the anterior pituitary substance called the adrenotropic hormone definitely increases the production of this principle by the adrenal cortex has, I feel, been demonstrated in cooperative experiments between our laboratory and that of the Mayo Foundation. If the position taken by Long in his debate with Houssay of Buenos Aires is correct, it should be possible to produce permanent diabetes by overconveyal of this hormone to normal animals as we were able to do with anterior pituitary extracts some years ago in Berkeley, and as has been recently more particularly studied by Young of London. This has not yet been accomplished, but it may be achieved in the near future.

DR. LESTER J. PALMER, Seattle: We have just heard a masterly summary of present knowledge of Addison's disease. I believe that the group of measures advocated—administration of salt and extract plus restriction of potassium—deserve endorsement and trial. This belief is based on the fact that the recommended regimen includes all the therapeutic agents indicated by our present knowledge. At the Mayo Clinic only eighty-nine cases have been observed in eighty-six months, or about one new case a month. In Seattle, in eight hospitals representing a capacity of 1,800 beds, where diagnoses have been indexed for periods varying from five to seventeen years, a diagnosis of Addison's disease has been recorded only twenty-six times. The bureau of vital statistics for the state of Washington (population 1,700,000) shows that for the five year period 1933-1937 Addison's disease appeared as a primary or contributory cause of death only twenty-five times. I believe these figures are really higher than the true figures would be. It should be mentioned that there is duplication of cases in the various series. At least two of the Seattle cases are known to be included in the Mayo Clinic group. Is this low incidence of Addison's disease apparent or real? Are patients dying in acute crises of Addison's disease, either as medical deaths or following surgical procedure, without being recognized? There is available the method of subjecting the suspected patient to test conditions outlined by Cutler, Powell and Wilder, which is apparently a safer procedure than that previously employed. May it not be possible that earlier diagnoses will become a fact and that a not inconsiderable number of patients who would previously have died in unexplained circulatory collapse will now be recognized as having Addison's disease?

DR. W. O. THOMPSON, Chicago: I should like to emphasize what Dr. Rynearson has said about the treatment of a crisis, which in Addison's disease presents an emergency fully as great as if not greater than that presented by diabetic coma. When a crisis has advanced to the point of unconsciousness, it is usually impossible to revive the patient with any form of therapy. I should like to stress the importance of large doses of adrenal cortex extract as well as of sodium salts in the treatment of a crisis in Addison's disease. I have used as much as 150 cc. of adrenal cortex extract in the course of the first twenty-four hours, a much larger dose, of course, than is required later for maintenance. Dr. Rynearson has already told you that at the Mayo Clinic they administer as much as 60 cc. of extract in the course of the first hour or two and then give an additional 30 or 40 cc. Early in a crisis a patient may be revived by the use of 40 or 50 cc. of extract alone, but if a crisis is well advanced it is necessary to add sodium salts, because the reserve of sodium in the body is depleted.

DR. EDWARD H. RYNEARSON, Rochester, Minn.: All of us are grateful to Dr. Evans for his remarks. The greatest advances in the treatment of Addison's disease have come from the laboratories and I am hopeful that work now in progress in Dr. Evans's laboratory may help further. Many patients suffering from either overfunction or underfunction of various endocrine glands enjoy periods of spontaneously improved health. Dr. Palmer referred to an interesting patient. If we can accept the diagnosis of Addison's disease as accurate, then we should be able to prophesy that with his present careless

attitude he is riding for a fall. If I were asked to guess the explanation for this patient's improvement, I should say that he probably has had some regeneration of the adrenal cortex. This is not unknown. Dr. Thompson's discussion is appreciated because of the fine work he has done in the study of this disease, which has just been reported before the the Association for the Study of Internal Secretions.

ANATOMIC FACTORS IN PATHOGENESIS AND TREATMENT OF URETHROCELE AND CYSTOCELE

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The levator ani muscles and their fascia have been generally conceded to be the essential supports of the urinary bladder.

Cystocele has been recognized to be a true hernia of the bladder—more specifically, a herniation of the fundus and trigon, which are those parts in association with the anterior vaginal wall.

The degree of incontinence of urine is evidently dependent on whether there is a urethrocele, which may or may not be associated with a cystocele, and varies enormously in different cases. It has been generally accepted that the specific anatomic lesion responsible for the incontinence is relaxation of "the sphincter muscle," yet most physicians have had a rather vague picture of the sphincteric anatomy and a very meager knowledge of the physiologic mechanism of vesical control.

The modern conception of correction of a cystourethrocele with incontinence has been that of repair of a hernia, with reenforcement of the urethral and trigonal support; but the anatomy of the structures used in the support of the mobilized and replaced and more or less incontinent bladder and urethra has not been well understood.

I believe that we have found answers to the major queries which arise in relation to these problems. The answers were inadequate after a concerted attack from the combined points of view of the anatomist and the gynecologist, despite painstaking expert dissection of the pelves of five selected female bodies; it was only after a sixth dissection was made, this time from within the pelvis in the case of a remarkably favorable specimen, that the anatomic relationships were revealed clearly and unmistakably.[1] The accompanying illustration is Tom Jones's depiction of the anatomy of cystourethrocele as viewed from the vaginal aspect at operation.

ANATOMY

Let us view the dissected pelvis from within, with the viscera, the parietal peritoneum and the pelvic cellular tissue removed, only the lower part of the bladder, much of the vagina, and the terminal portion of the rectum remaining: The endopelvic fascia is readily recognized, without effort, as the reflection upward on the viscera of the firm fascial layer covering the pelvic floor. An aponeuroticofascial ridge sweeps forward from the region of the spine of the ischium and soon divides into an inferior fascial arch, the white line, and the somewhat more superiorly placed, slightly curved arcuate ligament.

The dissection, if skilfully performed, reveals firm fascia ensheathing the bladder and the vagina, with a more delicate similar envelop for the rectum. The fascial tubes are the endopelvic fascia.

The anterior vesical reflection of the endopelvic fascia, i. e. the pubovesical fascia, creates a vesical sling from the pubis. The portion of the enveloping vesical layer on the vaginal aspect of the bladder is in intimate relation with the musculature of the bladder wall. A similar, less marked relationship is found between the vaginal reflection of fascia and the musculature of the vaginal wall. Thus there is a double layer of fascia between the bladder and the vagina, and each receives some muscle fibers from the wall of its adjacent viscus. The ensheathing fascia surrounding the viscera is firm and adds materially to their support. It begins on each viscus at the bottom of the pelvic cavity, and therefore the lowermost vagina and the lowermost urethra are not enveloped by the endopelvic fascia.

On removal of the fascia which lines the pelvic floor and its visceral reflections (the endopelvic fascia) and on excision of the viscera to a lower level, the levatores ani and coccygei, originating from the posterior aspect of the superior pubic ramus, the arcuate ligament (not the white line) and the spine of the ischium are seen to pass mediad and backward bilaterally, chiefly anteroposteriorly, toward the anococcygeal raphe and the sacrum. As the levatores ani sweep past the viscera, broad straplike bands of fibers are inserted into the lateral aspects of the rectum and the vagina, furnishing firm supports; an almost negligible number of strands are inserted into the posterolateral aspects of the urethra.

With the bladder excised down to the vesical neck, the urethra is seen as a thick walled shaggy tube, 1 cm. or more in diameter, its wall comprised of intrinsic muscle fibers which constitute the internal sphincter, naturally in a state of tonic contraction and in control of the normal accumulation of urine. One now sees the uterosacral ligament-like portions of the urogenital diaphragm arising from the pubis and firmly inserted into the lateral aspects of the urethra.

The urogenital diaphragm, or triangular ligament, at a lower level and anterior to the pelvic diaphragm, completes the pelvic support. With the urethra and the right half of the vagina excised to a still lower level and the levator ani and fascia removed from the right side, there is exposed the large ischiorectal fossa, anterior to which is the broad firm transverse musculomembranous urogenital diaphragm arising from the inferior rami of the pubis and ischium, stretched across almost the entire anterior half of the pelvic outlet at right angles to the vaginal canal. The muscles of the urogenital diaphragm constitute the external sphincter of the urethra. The muscle fibers of the diaphragm are directed chiefly transversely toward the midline, where they encounter the vagina and the urethra and are inserted firmly into them. As they meet the urethra many fibers are applied to it, inserted lengthwise along its distal portion, difficult to distinguish from the urethral fibers of the internal sphincter. A most prominent portion of these fibers in intimate relation with

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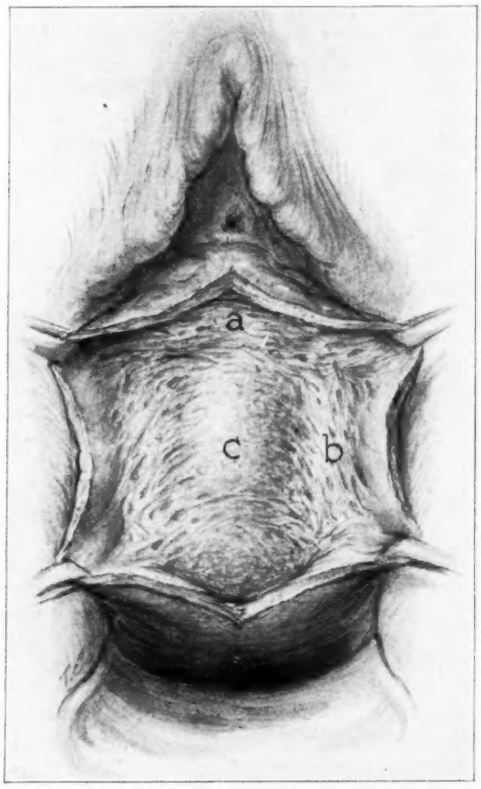
1. Three anatomically accurate illustrations of this dissection in its various stages will accompany another contribution, now in preparation.

the urethra consists of paired bands of the glistening superior fascia and underlying muscle fibers of the diaphragm arising bilaterally from the inferior pubic ramus near the midline and inserted into the anterolateral aspects of the urethra, presenting a miniature counterpart of the uterosacral ligaments. Some of the fibers of the diaphragm reach the midline beneath the urethra, but they form an insignificant layer here, in contrast with the lateral firm portions of the diaphragm.

It is my purpose to avoid discussion of a controversial subject; yet I must mention that microscopic study was made of tissue removed from several patients during operations on cystoceles. Generous blocks of firm supporting tissue excised from various locations during the operative dissections invariably contained much connective tissue, almost always in preponderance over the muscle fibers; the latter varied in amount according to the individual patient and the region from which the tissue was excised.



Pathologic anatomy of cysto-urethrocele as viewed from the vaginal aspect at operation: *a*, urogenital diaphragm, attenuated beneath the urethra and thick laterally; *b*, musculofascial vaginal envelop; *c*, musculofascial vesical envelop.

PATHOGENESIS OF CYSTO-URETHROCELE

What happens when a major lesion develops, such as a uterine prolapse together with a cystocele?

With the traumatisms of childbirth there is a rending of the supporting pelvic tissues, both muscles and fascia, and thenceforth the pelvic viscera sag. The lesion varies according to numerous undiscussed factors involved, such as the size, structure and axis of the bony and ligamentous framework and the size of the fetus, the presentation and the method and rapidity of delivery. Anatomic dissection emphasizes the importance of the fascial supports, a fact borne out by clinical experience when one demonstrates at complete hysterectomy the important supporting power of Mackenrodt's ligaments, which are nothing more nor less than reflections of fascia accompanying the uterine artery and vein.

Childbirth injuries are often comparable with those of an explosion—a generalized stretching, sagging and dragging. With such a lesion it is self evident that all the supporting tissues, far and near, play a part in the pathologic picture.

Uterine prolapse alone may occur with nothing more than stretching of the fascia which lines the pelvic floor, the uterovaginal fascial envelop with its associated muscle fibers and the all important perivascular fascia, known as Mackenrodt's ligaments, which extend, fan shaped, within the folds of the bases of the broad ligaments from the sides of the cervix and uppermost vaginal wall to become attached to the lateral bony walls of the pelvis.

If the lesion is essentially a cystocele or a cystourethrocele the disorder is more localized than with uterine prolapse, is lower and more anterior and may spare Mackenrodt's ligaments and the levator ani muscles including their straplike attachments to the lateral aspects of the rectum and the vagina. And, contrary to accepted belief, an extensive cystocele may develop solely as a result of rending and tearing and relaxation of only the pubovesical fascia and the fascial layers between the bladder and the vagina together with the urogenital diaphragm.

In the case of urethrocele alone, stretching of the fascia which ensheathes the intrapelvic urethra and tearing of the urogenital diaphragm away from the pubic bone are the dominant and sometimes the exclusive lesions, with resultant prolapse of the urethra downward and forward.

NERVOUS MECHANISM OF THE BLADDER

The nerve supply and nervous mechanism of the bladder have been worked out fairly satisfactorily, although incompletely:

The sensation of pain travels exclusively through the sympathetic fibers, which pass upward by way of the presacral nerve (the superior hypogastric plexus).

It appears that the mechanism concerned with normal filling and emptying of the bladder resides chiefly in the involuntary muscle of the bladder wall, which includes the circular thickened band of fibers of the vesical neck and urethra, termed the internal sphincter.

The motor nerve supply concerned with this mechanism comes through the paired erigens nerve, otherwise known as the erectile or pelvic nerve, the fibers of which emerge from the spinal cord in the anterior roots of the second, third and fourth sacral nerves and reach the bladder by way of Frankenhäuser's plexus. The afferent impulse to the cord concerned with the normal act of micturition probably travels through the pudendal (pudic) nerve, which reaches the perineum through Alcock's canal and carries afferent fibers to the cord through the second, third and fourth posterior sacral roots. The pudendal nerve also innervates the muscles of the urogenital diaphragm, including the external sphincter of the urethra.

Normally, the internal vesical sphincter is in a state of tonic contraction and controls the accumulation of urine. When the bladder becomes full an impulse to the cord stimulates the erigens (parasympathetic) nerve, with resultant relaxation of the internal sphincter, and at the same time a contraction of the remaining musculature of the bladder wall, thus emptying the bladder.

The external sphincter of the urethra plays no part in the normal control or emptying of the bladder; but it is called into play when the bladder becomes full, and it is all important in supporting the function of the internal sphincter in protecting against sagging and incontinence.

PRINCIPLES OF TECHNIC IN REPAIR OF URETHROCELE AND CYSTO-URETHROCELE

If there is a cysto-urethrocele alone, blunt dissection along fascial planes between the protruding bladder and the vagina and between the bladder and the uterus suffice to mobilize the herniating bladder.

The invariably recognizable musculofascial tissues between the vagina on one side and the bladder and urethra on the other are readily isolated by blunt dissection at operation and consist of the musculofascial components of the urogenital diaphragm below and the ensheathing layers of urethrovesical and vaginal fascia above, the double layered urethrovesicovaginal fascia strengthened by muscle fibers derived from these viscera.

The freed bladder may be held in replacement by suturing the bluntly dissected musculofascial supports. The union is accomplished by midline interrupted sutures, with more or less attachment to the uterus to accomplish satisfactory closure of the hernial opening. The more thoroughly one dissects the tissues well up over the urethra in the direction of the meatus, with suturing of the thinned-out and retracted musculofascial tissue lateral to the urethra to make a support beneath it, the more one may be assured of control of incontinence; unfortunately there is associated a longer period of time during which the patient will require catheterization.

Other lesions commonly accompany the cystocele. Relaxed Mackenrodt's ligaments may be strengthened by cutting the bases of the broad ligaments and suturing them together anterior to the cervix. For smoothness of workmanship in this detail, it is our custom to make a preliminary denudation of the overlying vaginal mucosa. The supporting pelvic floor should be repaired as a routine.

SUMMARY

Direct etiologic factors in the development of cysto-urethrocele are (1) relaxation of the fascia that lines the floor of the pelvis together with injury of its reflections (the endopelvic fascia), the bladder and the urethra, and the vagina, to the level of the floor of the pelvic cavity; (2) separation of the urogenital diaphragm from its firm attachment to the pubis, or stretching of the diaphragm, which permits the urethra to prolapse downward and forward.

Indirect etiologic factors in the development of cysto-urethrocele include (1) injury of the fascial reflections of endopelvic fascia which ensheathe the vagina posteriorly and the rectum, (2) relaxation of the strap-like bands of the levatores ani which firmly support the lateral aspects of the rectum and the vagina, (3) relaxation of more distant supporting structures, including the important Mackenrodt's ligaments and the levatores ani, especially the perineal portions of the latter.

In the controversial field concerned with the relative amount of fascial and muscle tissues present at dissection of a cysto-urethrocele, anatomic and clinical dissections and histologic study of excised pieces of tissue lead to the following deductions: The supporting tissue is predominantly fascia, but there is a generous amount of associated muscle fibers. Explanation of the derivation of this supporting tissue is as follows: The support in the region of the lower part of the urethra consists of the firm musculofascial tissues of the urogenital diaphragm, a part of which comprise the external sphincter; envelops of supporting fascia reflected from the fascia of the pelvic floor encase the bladder and upper part of the urethra and vagina, and these, particularly on the vesical aspect, are strengthened by muscle fibers derived from these viscera.

The repair of urethrocele can be best accomplished from the vaginal approach by blunt dissection along lines of musculofascial cleavage, according to the general principles of dissection, with musculofascial support derived from the tissues which have been described, according to the general principles of repair of hernia.

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ABSTRACT OF DISCUSSION

DR. W. T. DANNREUTHER, New York: The authors have clearly outlined the important factors concerned in injuries to the bladder and urethra resulting from birth trauma and indicated the structural principles involved in reparative operations. They have correctly called attention to the fact that a urethrocele is the prototype of a cystocele. The terms "urethrocele" and "prolapse of the urethra" are sometimes erroneously used interchangeably. A urethrocele involves all the walls of the urethra, whereas a prolapse is merely a protrusion of the mucosa through the meatus. This presentation is undoubtedly based on original dissections, which again emphasizes the importance of the endopelvic fascia as a supporting structure. It demonstrates that a cystocele without uterine prolapse may develop despite the integrity of the cardinal ligaments. Urine is normally accumulated in the bladder under a pressure of less than 10 mm. of water and is checked at the vesical orifice partly by the internal sphincter, which is simply a part of the detrusor smooth muscle fibers, and partly by the external sphincter, composed of striated fibers. Only the latter can be contracted voluntarily to prevent micturition when the bladder is full. The physiologic coordination of the detrusor muscle fibers and external sphincter, as well as normal balance of sympathetic and parasympathetic nerve impulses, is responsible for proper bladder control. Dysfunction eventuates in abnormal micturition. I agree with the authors that in doing plastic operations the dissection should be carried well over the urethra and the externally retracted tissues approximated snugly beneath it. In most cases of incontinence, two plicating mattress sutures of Pagenstecher linen, placed in the outer margins of the urethrocele itself, beneath the line of catgut sutures, will be found useful. Fixation of the anterior vaginal wall to the area on the cervix from which the prolapsed bladder has been freed and dislocated upward is prerequisite for the cure of large cystocele.

DR. G. D. ROYSTON, St. Louis: The type of cystocele and urethrocele, interdependent conditions, that I wish to add has to do with this trigonal muscle. This particular injury may be present when no cystocele or urethrocele can be made out from the outside, but can be recognized through a cystoscope aimed at the point where the muscle crosses the internal sphincter. When the patient strains, if this type is present, the floor of the bladder will be seen to go down, but the internal sphincter will not be materially depressed with it. In other words, as a result of the tear of the trigonal muscle near this point, the patient has a functioning cystocele only when she voids. This means that the trigon is functionally sheared from the internal sphincter, which becomes relatively free and therefore contracts, raises itself above the floor of the trigon and never is stretched downward or opened when the patient voids. This injury may be present with no other evidence of tearing or stretching of the musculofibrous bladder or urethral attachments. Consequently, the following changes occur: hyperplastic

urethritis and even caruncles, a protective mechanism of the internal sphincter due to friction of the mucosa within the spastic sphincter; also, secondarily, there is trigonal congestion with "sheep's wool" changes, i. e., desquamating epithelial cells or simply a passive congestion of the trigon extending over a long period. The presence of a caruncle may indicate dysfunction of the urethra. The liberated urethra shows various degrees of urethrocele. This relative liberation of the urethra is due to more or less complete functional section of the trigonal muscle, when the urethra is pushed upward and forward and its midsection is buckled or curved downward. The fixed external meatus becomes constricted and may occasionally form fibrous tissue and become strictured. Therefore there are a spastic external sphincter, a spastic internal sphincter, congestive trigonal changes, a change in the internal sphincter due to mucosal friction, and often a constricted meatus, fixed by the ligaments so well described by the authors. Dr. D. K. Rose of the Washington University School of Medicine and I have reported a method of repair of this type of injury which can be incorporated in any standard pelvic operation in suitable cases. This method aims to reunite the urethra functionally to the trigon. The operation deals principally with the longitudinal fibers mentioned and consists in inserting our sutures near the meatus, carrying them back to the midtrigonal region; then reinforcing the junction of the urethra and trigon and further reinforcing by repairing any posterior weakness in the bladder supports.

DR. JOSEPH L. BAER, Chicago: Some of these women who have been operated on and reoperated on still have either a complete incontinence or a degree of impairment which is almost as bad as incontinence itself. For these women there appeared in the *American Journal of Urology* approximately half a year ago an excellent and well illustrated article written by Dr. Lowsley. I have tried the operation twice since seeing the article. The last time was before the Chicago Gynecological Society. The essence of the operation is that an incision is made in horseshoe fashion enveloping the urethra and separating it from the symphysis pubis, a downward dislodgement, in other words, of the entire length of the urethra under procaine hydrochloride and epinephrine anesthesia, to which gaseous anesthesia may be added if desired. The entire space between the urethral and para-urethral tissues is dissected away from the symphysis pubis laterally, as wide as need be, until the junction of the bladder and urethra is freely exposed. Then, with the use of ribbon catgut, the lateral columns of the bulbus cavernosi muscles are brought together anterior to the urethra at the vesico-urethral junction in either a single tie or two such sutures, if desirable. Then the tissue over that is closed in the usual fashion and the horseshoe incision likewise closed with interrupted stitches and, if desired, a bit of rubber drainage. It seems to be efficient for those women in whom there has been considerable loss of tissue and in whom previous procedures by way of the vagina have failed.

DR. ARTHUR H. CURTIS, Chicago: From Dr. Royston's discussion I judge there is still some confusion relative to the anatomy of the internal sphincter. The musculature of the bladder wall constitutes the internal sphincter, which is not a circular band at the neck of the bladder but a thickening of the muscle fibers beginning at the neck of the bladder and extending throughout the urethra, reenforced by fibers from the urogenital diaphragm, which constitutes the external sphincter.

Number of Defectives Sterilized.—Of the twenty thousand persons operated on in the United States under the sterilization laws since 1907, the great majority have been mental patients. Only about one third of the total were feebleminded. It can be readily seen, therefore, that the number of mental defectives sterilized over a period of twenty-three years represents but a small fraction of 1 per cent of the present total in this country. Assuredly, then, sterilization has thus far proved a striking failure as a large-scale measure for cutting off defective stock. —Deutsch, Albert: The Mentally Ill in America, New York, Doubleday, Doran & Co., Inc., 1937.

LEVELS OF CONTROL IN THE TREATMENT OF DIABETES MELLITUS

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AND
ROBERT L. JACKSON, M.D.
IOWA CITY

For twelve years the treatment of diabetes mellitus in children in our clinic has been based on the premise that the diabetic child has normal propensities for health as long as his diabetes is controlled and that therapy should be based on the maintenance of physiologic conditions as far as possible. Prescribed diets have been planned to meet liberally all requirements for growth and activity. The dosage of insulin has been designed to control hyperglycemia at all times. Whereas the instability of the diabetic child does not permit the fullest attainment of this ideal, continuous approximation of normal blood sugar levels has been our criterion in judging the success of management. Effort has been made to avoid glycosuria of any degree as a regular or frequent occurrence. A regimen of management has been evolved which has made such a level of control possible when suitable supervision of the patient is maintained.

When protamine zinc insulin became available and reports of its superiority appeared in the literature, we were led to hope that through its use we might lessen the number of daily injections without lowering the level of control which had previously been established. For over a year the modified insulin has been used for selected hospitalized diabetic children. The regimen provided for strict control of the patient's activities as well as his diet and insulin. Competent laboratory personnel made analyses of all urine passed and of the sugar content of the blood at intervals throughout the twenty-four hours several days each week. Exercise was supervised and standardized as far as possible. From the technical standpoint, the routine employed was adequate to certify the validity of the data obtained. Preliminary to the use of modified insulin, each patient was observed under the earlier regimen with regular insulin, and the requirements of the latter had become essentially stable. The preliminary period averaged four weeks and for some patients was much longer. During this perod, once the patient had become aglycosuric a marked decline was noted in the total insulin needed to maintain normal blood sugar levels with a constant diet. Chart 1 illustrates the time factor involved in this process of stabilization and the degree of spontaneous reduction in the requirement of insulin which may be observed. To establish and maintain such stability it was necessary to give from two to four injections daily in accordance with a previously established distribution and to readjust the total dose frequently.

When these patients were transferred to protamine zinc insulin, great difficulty was encountered in attaining levels of control as good as those which had previously been established for the same subjects with regular insulin. If the urine was kept free from sugar the patients tended to have hypoglycemic shock of a type far more severe than that previously observed. With careful supervision it was possible to establish passable control

From the Department of Pediatrics, State University of Iowa College of Medicine.
Read before the Section on Pediatrics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

with the protamine zinc product for the children who required relatively small amounts of insulin; yet even with these children the status was less predictable than when regular insulin was used. At the termination of the study we were forced to conclude that the use of protamine zinc insulin for diabetic children is not compatible with the maintenance of physiologic levels of the blood sugar.

It is not our desire to condemn the use of modified insulins or to close our minds to their ultimate value in the treatment of children with diabetes. Our inability to use protamine zinc insulin successfully must not be accepted as evidence that in the hands of others it may not be used with success. However, other observers have reported difficulties similar to those we have encountered. The discrepancy between the favorable and the unfavorable reports is explainable by the differences in objective of treatment in various clinics or by the level of control maintained in the management of the disease.

At the outset of any discussion of the treatment of diabetes one should distinguish between the elderly patient, whose objective is to pass his declining days in comfort, and the younger patient, who wishes to participate in the various activities of life. Moreover, separate consideration must be given to the child or adolescent patient, who still has a capacity for growth, as opposed to the adult, who has achieved his maximum physique. If the patient offers no prospects of salvage, one may justifiably pursue a passive and lenient form of therapy. If, on the other hand, he has a capacity for health and a fair normality of existence, the physician should feel an obligation to treat the diabetes so effectively that it will offer a minimum of obstruction to his future progress. In treating the child, the routine

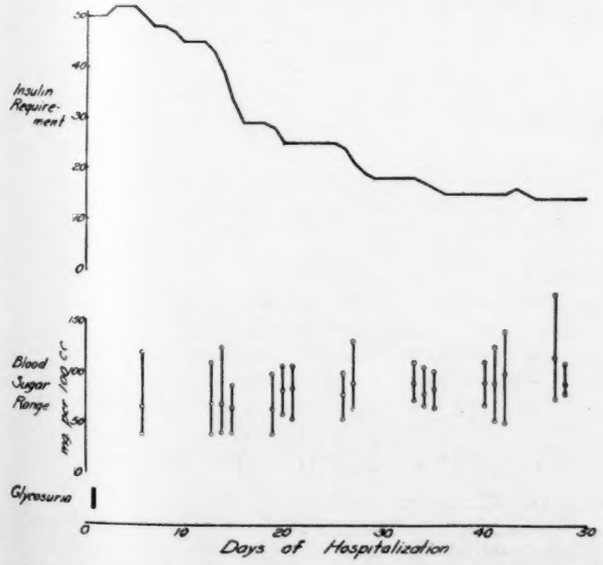

Chart 1.—The progressive and prolonged decline in the insulin requirement with a constant diet and maintenance of aglycosuria. The data are taken from the record of an 11 year old girl with diabetes of recent onset. The blood sugar values represent the maximum, minimum and average of nine determinations for each day where indicated.

and plan of control must be especially stringent if the patient is to have an opportunity for normal growth in body and in mind. A regimen which meets all needs of a child can be applied with equal value to the adult patient, whereas a lax or unphysiologic type of management which may be considered appropriate for certain mature patients will prove inadequate and a handicap in the care of the child. This distinction will not be immediately apparent clinically; the child may subsist without obvious handicap, and the parents and the attending physician may be led to believe that an ineffective regimen is meeting all the patient's needs. Long range studies are necessary to determine the relative worth or safety of different methods of treatment, and many factors must be considered in the establishment of adequacy of control.

In treating the patient with diabetes, one cannot hope for a cure. Under the best of management the patient's defect will persist in a significant degree, and realization of this must be kept uppermost in all future planning. The goal of treatment should be the conservation of the deficient sugar-handling function and the direction of the patient's medical and social status so that he may lead a full life. The ultimate outcome of the disease will be determined through the adequacy of the regimen to promote normal functioning of the body throughout and to prevent complications and degenerative sequelae. With adequate control the diabetic child has the propensity for normal growth, development and maturation. He will have the strength and ability to participate in the activities of his normal associates as long as they do not conflict with the regimen which his management necessarily imposes. He need not be subject to diastrous complications or sequelae, such as acidosis, diabetic cataracts, gangrene or hepatomegaly, if he adheres continuously to a suitable regimen. With a lax form of management it may appear that all these objectives are being attained; minor depression of growth or the development of degenerative changes may not become clinically apparent for a long period. Leniency in control may please the patient and his parents and may simplify the work of the physician, but ultimately it will result unfavorably for the patient.

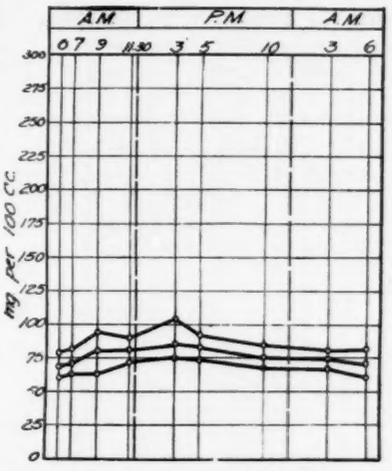

Chart 2.—Diurnal fluctuations of the blood sugar level in six nondiabetic children receiving diets similar to those of diabetic children but without administration of insulin. Nine determinations were made for each subject during two different twenty-four hour periods. The upper and lower curves represent the maximum and minimum values observed at each hour; the center curve represents the average of the twelve determinations.

The patient's sense of well-being and his clinical manifestations do not offer a safe guide as to the adequacy of his management. His sugar-handling mechanism may be markedly decompensated without causing noteworthy symptoms. The physician must interpret to the patient or his parents the need for continued periodic laboratory studies to confirm the level of control.

Many physicians treating patients with diabetes mellitus have no facilities for the determination of blood sugar and judge the progress of their therapy by occasional urinalyses and the patient's clinical manifestations. Under this type of regimen, glycosuria is common and inevitable. Frequently only a single voiding is tested, and the results do not reflect the status of the patient. Increasing severity of the diabetic state

will not be detected until it becomes apparent through aggravation of the patient's symptoms. This approach is negative and fails to offer the patient the safeguards which modern methods of treatment make available.

Some clinicians treating diabetes have questioned the harmfulness of mild glycosuria, even though it is persistent. They reason that, if the patient utilizes sufficient sugar for his body's needs, mild wastage can be ignored. This attitude is indefensible when one is outlining suitable management for the child with diabetes, since it is unnecessary, is theoretically unsound and clinically leads to the complications and degenerative sequelae which characterize uncontrolled diabetes.

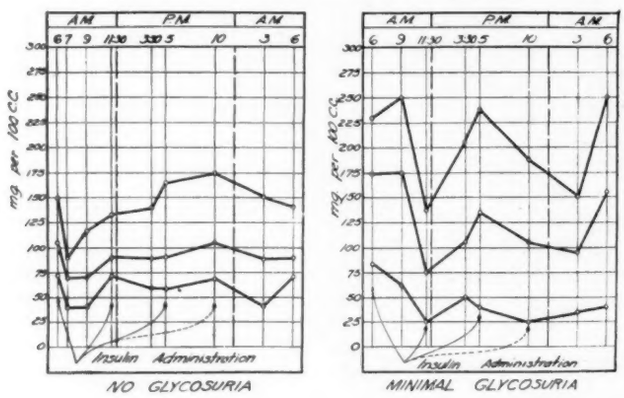

Chart 3.—Diurnal blood sugar fluctuations of mildly diabetic children receiving less than 30 units of insulin a day in three or four divided doses. The curves at the left represent seventeen days' study of four subjects who were aglycosuric. The curves at the right represent ten days' study of three patients who were excreting minimal amounts of sugar, not more than 5 Gm. a day. The upper and lower curves represent the maximum and minimum values observed at each hour; the center curve represents the average of all determinations made at that hour.

Charts 2, 3 and 4 illustrate that even the mildest glycosuria is not compatible with the maintenance of satisfactory blood sugar levels. Chart 2 shows the average diurnal fluctuations in the blood sugar level for a group of nondiabetic children. Chart 3 shows similar values for two groups of mildly diabetic children; some were aglycosuric and others were excreting a daily maximum of 5 Gm. of sugar. Chart 4 offers a similar comparison of blood sugar levels for children with moderately severe diabetes in the absence and the presence of minimal glycosuria.

Glycosuria is the sequel to hyperglycemia. The blood sugar concentration must reach abnormal levels before sugar appears in the urine. Before such levels are attained, the body's defenses will have attempted to prevent them and have failed. Such failure of a physiologic function constitutes a state of decompensation and is associated with pathologic fatigue of the agencies concerned in the maintenance of that function. Such exhaustion of the sugar-handling function accounts for a considerable part of the patient's insulin defect. This can be demonstrated through the degree of recovery observable in the diabetic patient brought under proper control; with the continued use of suitable amounts of insulin, the dose must be successively reduced as the exhaustion component becomes corrected through rest.

With prolonged hyperglycemia, the diabetic patient acquires a higher renal threshold for sugar. As a result he may remain persistently hyperglycemic without noteworthy glycosuria. Abnormally high levels of blood sugar, with or without glycosuria, cannot be considered physiologic, and one may expect that over long periods the chemical alterations in body fluids will lead to degenerative conditions in the tissues. Certain sequelae of diabetes, such as cataracts, hepatomegaly and xanthoma diabeticorum, are explainable on this basis. Ophthalmologists recognize the fact that the optical characteristics of the eye vary with the sugar content of the body fluids. The increased susceptibility of the diabetic patient to local infections is thought to be related to the effect of a high level of blood sugar. In our series of over 200 diabetic children, the only degenerative complications have occurred in those who had such manifestations at the time they first came under our observation or who failed to follow the prescribed regimen. Those who have shown reasonably good cooperation have not only been free from noteworthy complications and sequelae but frequently have attained a level of health superior to that of brothers and sisters living under the same adverse socio-economic conditions.

Attempts should be made to keep the diabetic patient free from glycosuria at all times and to avoid hyperglycemia. This goal may not be attainable, but the physician may approach it more nearly than is generally recognized. With a constant type of diet and with the doses of insulin distributed suitably throughout the twenty-four hours, the patient should avoid marked fluctuations in the blood sugar level. Under these conditions the physician can instruct the parent to maintain the child's doses of insulin at as high a level as is possible without the production of shock. This routine, checked through frequent urinalyses of samples voided at different times of the day, will safeguard the patient against undetected hyperglycemia. When mild shocks occur, they are easily controlled by the oral administration of minimal amounts of sugar. Such a regimen approximates physiologic conditions as closely as the patient's state will permit.

As a criticism of this strict level of control, the physician may with justice question whether the patient will adhere to such regimentation. We have found that it is no more difficult to work from the stated objectives than from a lower level of treatment. Each patient finally reaches a stage of compromise between that which is prescribed and that which his home environment makes possible. With the more favored patients, the compromise is a small one. With the noncooperative, economically handicapped or indifferent family,

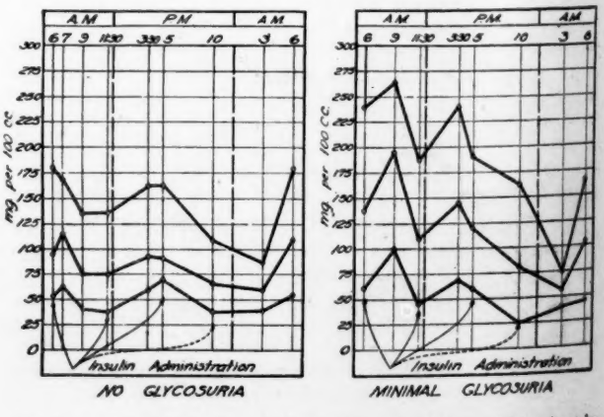

Chart 4.—Diurnal blood sugar fluctuations of children with moderately severe diabetes receiving from 30 to 60 units of insulin a day in four divided doses. Six aglycosuric subjects, with a total of nineteen days' observation, provided the data shown at the left; four patients with minimal aglycosuria (an excretion of not more than 5 Gm. in the twenty-four hours), with a total of ten days' observation, were used in the study illustrated at the right. The significance of each curve is as described under chart 3.

evidence often indicates that the regimen is being met in minimal degree. Even so, we feel it advantageous to prescribe nothing less than the best for the patient's ultimate interests; if compromise is to be made, let it be made by the patient and his parents, not by the physician. Although the patient may do less than we direct in the way of therapy, he is not likely to do more.

The regimen for treatment of the patient with diabetes should be directed toward the conservation of his resources in their entirety. This implies the maintenance of aglycosuria as far as possible. A regimen which requires or condones glycosuria, even of mild degree, cannot be considered favorable for the patient's ultimate welfare.

ABSTRACT OF DISCUSSION

DR. PERCIVAL ALLEN GRAY JR., Santa Barbara, Calif.: The aim in the management of the diabetic child is to provide a diet adequate for growth and development and to maintain a blood sugar level within physiologic limits. Before the advent of modified insulin four hypodermic injections a day were usually required to realize this aim. Without a fourth, or nocturnal, dose of insulin the child could not consistently maintain a normal fasting blood sugar level. The use of modified insulin has obviated the necessity for so many doses. The policy at the Santa Barbara Clinic has been to administer before breakfast the least amount of protamine zinc insulin necessary to control hyperglycemia during the ensuing night. When this amount has not also sufficed to control hyperglycemia during the day, supplementary doses of unmodified insulin have been given. Few of the children have been able to stay controlled with one dose of protamine zinc insulin a day. The majority have required at least one supplementary dose of unmodified insulin, which has usually been given at the same time in the morning. This program has reduced the danger of unrecognized hypoglycemic shock to a minimum. The necessity of giving a quick-acting insulin with the more slow-acting preparation is occasioned by the delayed absorption of the latter. Since histon insulin contains a greater proportion of free insulin per unit volume than does protamine zinc insulin, it does not have to be supplemented with unmodified insulin as often. Each preparation is capable of controlling juvenile diabetes when used alone. However, in many instances the amount required may be so great as to subject the patient to a grave risk from hypoglycemic shock. This risk is increased by the unpredictability of the absorption of modified insulins. One is often forced to weigh the risk of chronic hypoglycemia against that of chronic glycosuria. Many patients are not suited to treatment with modified insulin and must return to multiple doses of unmodified insulin. Some patients do well only if their modified insulin is supplemented by multiple doses of unmodified insulin. One wonders what advantage accrues if the child requires three or four injections anyway. I agree with the authors that protamine zinc insulin has been something of a disappointment in the treatment of juvenile diabetes cases. Not only has it frequently failed to prevent the characteristic wide fluctuations in the blood sugar level, but it has produced some troublesome local cutaneous reactions. Some children who at first did poorly with protamine zinc insulin did well later when their diet was changed. At present my associates and I consider from 200 to 225 Gm. of carbohydrate the upper desirable limit for patients receiving modified insulin. This carbohydrate allowance is given one fifth for breakfast and two fifths for each of the other two meals. Bedtime nourishment has been insisted on to protect against hypoglycemia during the night. I feel strongly about negligent treatment of diabetic children, but much of my early fear about the deleterious effects of mild, even though persistent, glycosuria has faded. Children seem to grow at a normal rate, pass successfully through accidents and illnesses, avoid the classic complications of diabetes and lead happy and useful lives in spite of never being exactly sugar free.

DR. LEONA M. BAYER, San Francisco: This paper seems important in relation to certain problems which I have found in the care of diabetic children at Stanford University Hospitals. With so much medical publicity in newspapers, a curious situation seems to be springing up, in which the burden of proof is on the physician who does not immediately subscribe to all the newest methods. Thus the physician who says that protamine zinc insulin is often not appropriate or that strict control is valuable, in spite of much discussion of free regimens, is sometimes put on the defensive. For this reason such a critical evaluation of the effect of protamine zinc insulin based on a preliminary demonstration of the changes in the level of control under careful supervision with regular insulin seem to me most valuable. Before the long time value of strict versus less rigid control can be definitely proved, longitudinal studies on diabetic children are needed for comparison with the normal growth studies which are now coming out of child study institutes.

DR. J. D. BOYD, Iowa City: With the use of regular insulin and a strict regimen of management, an excellent level of diabetic control can be maintained, with essential freedom from glycosuria, even with the severely diabetic child. Protamine zinc insulin can do no more than this, and in our hands it has been less effective. However, we are concerned less with the problems of protamine zinc insulin than with urging adherence to higher standards of treatment for the child with diabetes mellitus.

GASTRODUODENOSTOMY FOR CERTAIN DUODENAL ULCERS

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AND
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Although the operation of gastroduodenostomy was suggested in 1892 by Jaboulay [1] and first applied in 1898 by Henle,[2] it has received no widespread application and in fact is unknown to many surgeons. This is a curious circumstance to us, for although gastroduodenostomy is by no means a panacea for all duodenal ulcers, there are certain situations in which it can be readily applied with most satisfactory results. It is not our intention at this time to enter the controversy which still continues regarding the relative advantages

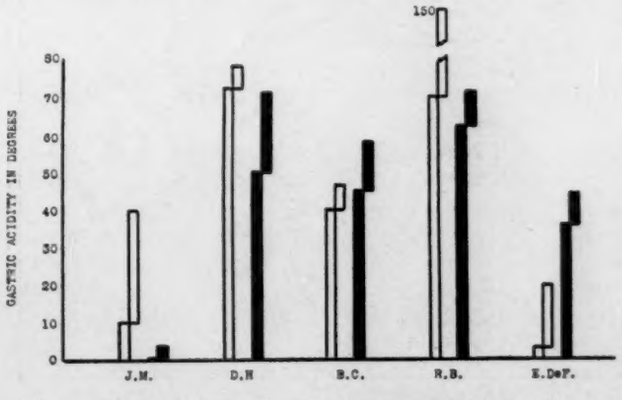


Fig. 1.—Degrees of free and combined gastric acidity for five patients before (hollow blocks) and after (solid blocks) lateral gastroduodenostomy.

of short-circuiting operations and some type of gastric resection for duodenal ulcer. It is generally recognized that duodenal ulcers which finally require surgical intervention because of the failure of medical treat-

Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Jaboulay, Mathieu: De la gastro-duodenostomie, Arch. prov. de chir. **1**: 551, 1892.

2. Henle, A.: Ein Fall von Gastroduodenostomie, Centralbl. f. Chir. **25**: 753, 1898.

ment or because of the occurrence of complications during their course cannot all be managed by any one surgical procedure. The surgeon must be prepared in each case to apply the operation best adapted to the conditions encountered. Some patients should certainly have a subtotal resection of the stomach, and for others it is recognized that some type of short-circuiting operation is best. Gastroduodenostomy is one of the short-circuiting procedures which has an occasional place in the surgical treatment of duodenal ulcer.

Since the successful beginning of gastrointestinal surgery in 1881, with Woelfler's gastrojejunostomy and the Billroth I gastric resection, many operations for the treatment of duodenal ulcer have been devised. Surgeons at first concerned themselves chiefly with gastrojejunostomy and various combinations of this operation with gastric resection. Later they focused their attention on operations involving only the stomach and duodenum, including the pyloroplasties described by Heineke in 1886, Finney [3] in 1902 and Horsley [4] in 1919.

Jaboulay [1] in 1892 first suggested anastomosis of the stomach and the second part of the duodenum. He pulled the anterior surface of the stomach down and over to the right, so that the anastomosis was difficult

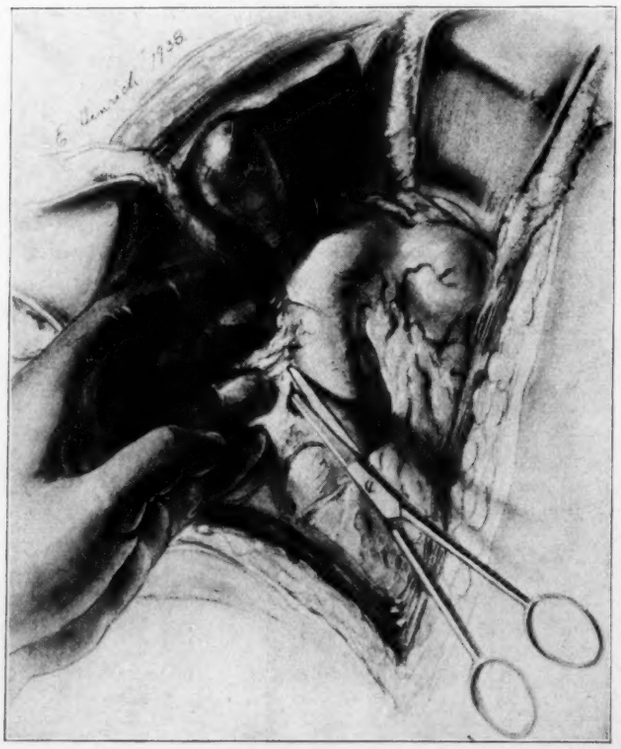


Fig. 2.—Mobilization of the second part of the duodenum by cutting the parietal peritoneum at its posterior border is the first essential in gastroduodenostomy.

of performance and resulted in tension on the suture line. Villard [5] in 1900 reported an easier modification, much more like the one we use today, in which the duodenum was made to anastomose with the right end of the greater curvature of the stomach. Theodor Kocher [6] in 1903, however, was the first to mention specifically the feature of modern gastroduodenostomy which makes its performance so easy and so satisfactory: complete mobilization of the second part of the duodenum simply by incision of the parietal perito-

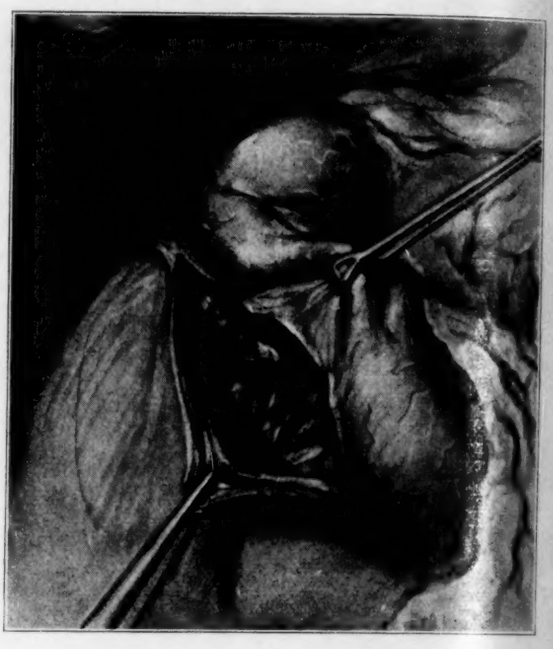


Fig. 3.—The wrong way to turn the duodenum over to the stomach. When the lateral side of the duodenum is grasped rotation occurs, with resulting obstruction.

neum lateral to it. It is of interest that Kocher, master surgeon, wrote of gastroduodenostomy: "We regard it as the normal procedure, and we are of the opinion that it will take precedence over all the previous methods of gastro-enterostomy and pyloroplasty." The operation of Villard as modified by Kocher and the procedures described by Balfour [7] in 1918 and by Moynihan [8] in 1921 differ in only minor particulars from the technic we follow today.

Rienhoff [9] in 1932 described an "infrapapillary gastroduodenostomy," in which the gastric contents are emptied into the duodenum well below the papilla of Vater. It is not apparent to us that sufficient advantage comes from entering the duodenum in its third part rather than its second to warrant the added dissection necessary to mobilize it.

Much work has been done on the subject of gastric acidity and its changes after various stomach operations, particularly those designed for relief or cure of duodenal ulcer.

Snell [10] has recently emphasized, and Steinberg, Brougher and Vidgoff,[11] Hill, Henrich and Wilhelmj,[12]

3. Finney, J. M. T.: A New Method of Pyloroplasty, Bull. Johns Hopkins Hosp. **13**: 155 (July) 1902.

4. Horsley, J. Shelton: A New Operation for Duodenal and Gastric Ulcer, J. A. M. A. **73**: 575 (Aug. 23) 1919.

5. Villard, Eugene: La gastroduodenostomie sous-pylorique, Rev. de chir. **22**: 494, 1900.

6. Kocher, Theodor: Mobilisierung des Duodenum und Gastroduodenostomie, Zentralb. f. Chir. **30**: 33, 1903.

7. Balfour, Donald C.: Gastroduodenostomy, Indications and Technic, Ann. Surg. **67**: 80 (Jan.) 1918.

8. Moynihan, Sir Berkeley: Abdominal Operations, ed. 4, Philadelphia, W. B. Saunders Company, 1921.

9. Rienhoff, W. F.: Infrapapillary Gastroduodenostomy by Mobilization with Retromesenteric Displacement of the Duodenum and Jejunum, Ann. Surg. **95**: 183 (Feb.) 1932.

10. Snell, Albert M.: Behavior of Stomach After Operation for Duodenal Ulcer, Am. J. Surg. **35**: 45 (Jan.) 1937.

11. Steinberg, M. E.; Brougher, J. C., and Vidgoff, I. J.: Changes in the Chemistry of the Contents of the Stomach Following Gastric Operations, Arch. Surg. **15**: 749 (Nov.) 1927.

12. Hill, F. C.; Henrich, L. C., and Wilhelmj, C. M.: Changes in Gastric Acidity After Various Operations, Arch. Surg. **31**: 622 (Oct.) 1935.

Walters,[13] J. M. T. Finney Jr.[14] and others agree, that the reduction in acidity often obtained after pyloroplasty, gastroduodenostomy or gastrojejunostomy and even that following subtotal gastric resection is due chiefly to regurgitation of the duodenal contents. Furthermore, as Wilhelmj, Henrich and Hill[15] have pointed out, the efficiency of duodenal secretions in lowering the acidity in the stomach is perhaps due 75 per cent to simple dilution and only 25 per cent to neutralization. Hill and his associates, using dogs, showed that the increase in duodenal regurgitation was maximal after gastroduodenostomy, more than after either gastrojejunostomy or pyloroplasty.

From the physiologic point of view it would appear logical to empty the acid gastric secretion into the duodenum rather than into the jejunum. It is now common clinical knowledge that the farther away from the pylorus the gastric juice enters the intestine, the greater the chance for suture line ulceration. This has recently been again confirmed in the laboratory by de Bakey.[16] He showed by a series of experiments that, with gastrointestinal anastomosis, ulceration occurred in a steadily rising percentage of cases when increasing quantities of the bile, pancreatic juice and succus entericus were removed from the area of the suture. He found suture line ulcer in 100 per cent of those animals in which no bile, succus entericus or pancreatic juice reached the suture line. In view of these and similar experiments it would seem that gastroduodenostomy should seldom be followed by anastomotic ulcer

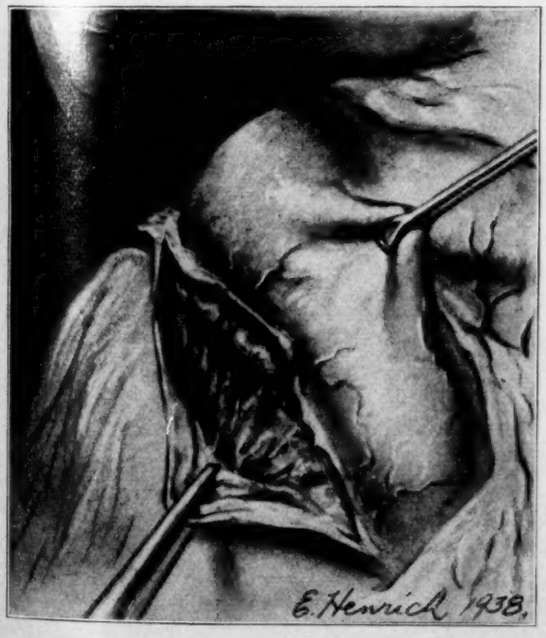


Fig. 4.—The proper way to lift the second part of the duodenum bodily over toward the stomach. When adequate mobilization has been secured this can be done with no tension whatever on the duodenum.

and should be a valuable means for neutralizing high gastric acidity by permitting alkaline duodenal contents readily to enter the stomach. That gastric acidity is lowered by gastroduodenostomy, however, is by no means clear from our results.

The accompanying chart of gastric acidity for five of our patients who had gastroduodenostomy shows no evidence of adequate dilution of neutralization of gastric acidity. As may be seen, the total and free acid from months to years after operation was nearly as high as or

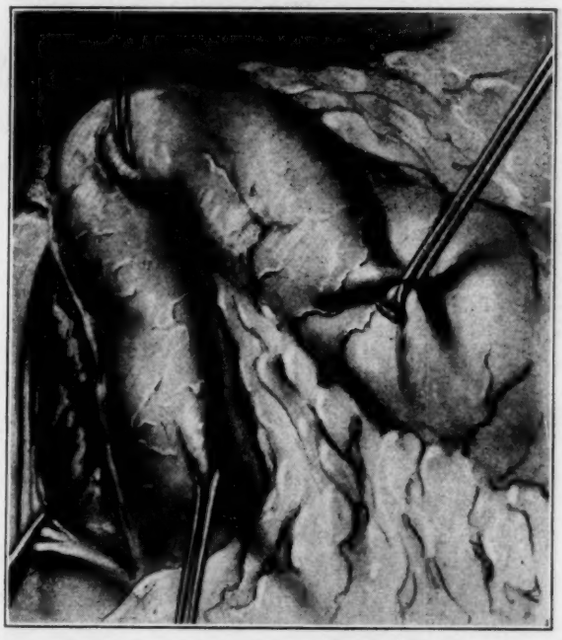


Fig. 5.—The duodenum brought up toward the greater curvature of the stomach, which is now readily laid against it.

was higher than it had been before operation. This we find very surprising, since all the patients are clinically apparently well and recent x-ray studies show no evidence of any pathologic change.

Theoretically, anastomotic or suture line ulcer either should not occur or should be very infrequent after gastroduodenostomy, but in actual practice it occasionally does occur. We doubt that it is frequent, but it is difficult to obtain any statistics. Moynihan never saw secondary ulceration. J. M. T. Finney Jr. said that anastomotic ulcer does not follow gastroduodenostomy. Flint,[17] in a study of 200 operations, did not see this complication. We have had no evidence of suture line ulcer in our fifteen cases.

That suture line ulcer may follow gastroduodenostomy, however, is attested by Wilkie's[18] report in 1933 of two cases in a series of 159 gastroduodenostomies. He said, however, that in both cases the ulcer responded immediately to later gastrojejunostomy. More recently Graham[19] reported one stomal ulcer in his experience with nine gastroduodenostomies. We have therefore positive evidence from the literature of only three stomal ulcers after nearly 400 operations, an incidence of less than 1 per cent. Allowing for inaccuracies, this is still a considerably lower incidence of stomal ulcer than the 8.5 per cent reported in England by a careful collective inquiry into gastrojejunal ulcer after posterior gastro-enterostomy.[20]

13. Walters, Waltman: Gastric Acidity Following Operations for Gastric and Duodenal Ulcer, Ann. Surg. **104:** 585 (Oct.) 1936.
14. Finney, J. M. T., Jr.: Pyloroplasty and Gastroduodenostomy, Surgery **2:** 738 (Nov.) 1937.
15. Wilhelmj, C. M.; Henrich, L. C., and Hill, F. C.: The Influence of Duodenal Secretions on Acid Gastric Contents, Am. J. Physiol. **111:** 293 (March) 1935.
16. de Bakey, M. E.: Peptic Ulceration, Arch. Surg. **34:** 230 (Feb.) 1937.
17. Flint, E. R.: Further Experiences with Gastroduodenostomy, Lancet **1:** 12 (Jan. 1) 1927.
18. Wilkie, D. P. D.: Indications for Surgical Therapy in Peptic Ulcer, Brit. M. J. **1:** 771 (May 6) 1933.
19. Graham, Roscoe R.: Technical Surgical Procedures for Gastric and Duodenal Ulcer, Surg., Gynec. & Obst. **66:** 269 (Feb. 15) 1938.
20. Wright, Garnett: A Collective Inquiry by the Fellows of the Association of Surgeons into Gastrojejunal Ulcer, Brit. J. Surg. **22:** 433 (Jan.) 1935.

Gastroduodenostomy has thus far been most satisfactory in our experience in the relief of pyloric stenosis. We have used it in seven cases of this condition in the last three and a half years, with results that have been most satisfactory. Four of the seven patients were in a serious condition when admitted to

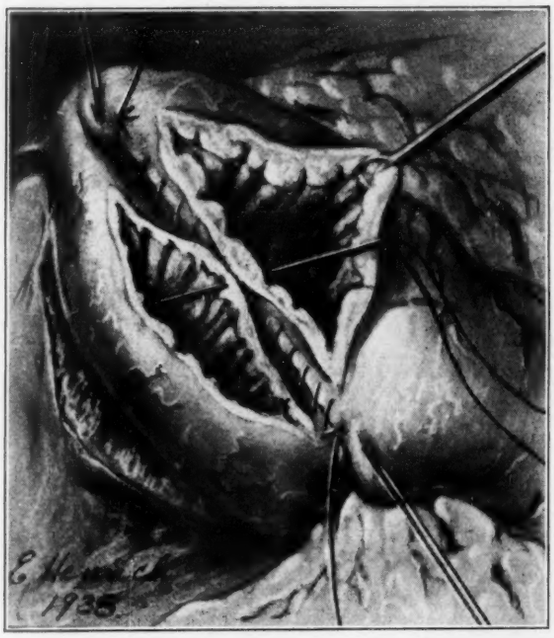


Fig. 6.—The posterior layer of silk sutures has been inserted; the stomach and the duodenum have been opened, and the inside layer of sutures is started.

our service. They were all over 50, one being 67. The four all showed clinical and chemical evidences of their long-standing obstructions. One patient, a woman, was confused, disoriented and semicomatose, with a high nonprotein nitrogen content, a high value for carbon dioxide and a low content of blood chlorides. We spent ten days preparing her for operation, and in addition to a gastroduodenostomy we did a jejunostomy, by means of which immediate postoperative feeding was given. We have repeatedly used jejunostomy for feeding in cases of serious involvement of the stomach and are convinced that it is a valuable adjunct in their management.

The postoperative course of these patients with obstruction was surprisingly comfortable. Almost no vomiting occurred, and gastric drainage by Levine tubes was usually unnecessary after a few hours. Their course seemed to us much smoother than that of patients with a similar involvement who had had a posterior gastro-enterostomy.

All these patients are still feeling well after intervals of six months to three years. Roentgenograms show the new stoma working well, with varying amounts of barium sulfate going through the pylorus. Four had their gastric acidity checked a year or more after operation. To our surprise it was higher than normal in three cases and normal in the fourth. This fact causes us some concern as to future possibilities in spite of the present comfortable clinical status of the patients.

We have used gastroduodenostomy for two patients, both men, who had persistent pain from duodenal ulcer in spite of long medical treatment. They have been relieved of their symptoms and apparently are doing well one and two years, respectively, after operation, although one showed a high value for total acid when examined a year after operation. This man's fluoroscopic examination showed most of the barium sulfate going through the new opening and a two to three hour emptying of the stomach. Because of the high gastric acidity persisting after operation in this case and in others we have observed, we are hesitant to use this operation for the nonobstructed duodenal ulcer for which medical management fails, in spite of the present comfort of both these men. We would, we believe, feel much more optimistic as to their future if we had done a subtotal gastrectomy.

We have done gastroduodenostomy for two male patients with duodenal ulcer who had had serious hemorrhages. One of these has remained entirely comfortable and very well for over two years. The other patient died a few hours after operation.

There is an increasing tendency among surgeons to operate when there is massive hemorrhage from duodenal ulcers if the patient's condition warrants and to resect the stomach and the ulcer if possible. We are in agreement with this policy when it can be followed, but certainly we believe that in many hands radical resection of the stomach just after acute bleeding will carry a serious mortality. Furthermore, it is well known that in occasional instances a short-circuiting operation has been beneficial. Gastroduodenostomy may permit one to view the bleeding ulcer when the duodenum is opened and may permit suture of its base. This procedure is certainly not ideal for the complication, but we believe that for certain bleeding ulcers

Fig. 7.—From a recent case of gastrojejunal and duodenal ulcer in which repeated serious hemorrhages occurred. In such cases the gastrojejunostomy must be taken down, the jejunum closed and either a subtotal gastrectomy performed or some other procedure like gastroduodenostomy done to overcome pyloric spasm and obstruction.

the patient's condition, the ulcer's location and the surgeon's abilities combine to make it a most useful operation.

In two cases we have combined gastroduodenostomy with the resection of an ulcer very high on the lesser curvature of the stomach. The first operation was

done over two and one-half years ago; the patient was a man of 58 and has been repeatedly examined by x-rays and gastroscopy. For a year after operation he was well in every way and his ulcer had healed. He then had a return of the ulcer in the lesser curvature, where it was previously excised. There has been much question as to whether or not it is malignant, but since it has not changed in some months it is apparently benign. The other patient was a girl of 18 with a perforating ulcer very high on the lesser curvature, which we felt was too indurated to permit subtotal gastrectomy. Her operation was recent and she is still doing well.

From these experiences we feel that we cannot recommend, as first choice, gastroduodenostomy and local resection of ulcers high on the lesser curvature. We believe they should have subtotal resection of the stomach if feasible. If resection is not safe, however, as in our second case, we believe that local resection by knife or cautery, plus some short-circuiting procedure, is the only choice.

Gastroduodenostomy has been particularly helpful to us in the successful management of two bleeding gastrojejunal ulcers. Our experience with such ulcers has frequently been distressing because of the extensive surgical procedures necessary to cure them. Ideally certain fundamental steps are desirable and necessary. One must (1) remove the jejunum from the stomach, (2) remove any ulcer from the jejunal wall and close the jejunum and (3) overcome pyloric obstruction and high gastric acidity either by resection of the stomach or by some short-circuiting procedure.

The addition of a subtotal gastric resection and a Polya or other anastomosis to the removal and repair of the jejunum is at times, in our opinion, too much surgical intervention. We have in the past, in one case, taken down the gastro-enterostomy and left the duodenum alone. The patient, a man, later had severe pyloric obstruction, had a gastric resection elsewhere and died. It is apparent to us, therefore, that after the reduction of a gastro-enterostomy relief of pyloric spasm and obstruction must be assured by either a plastic operation on the pylorus or a subtotal gastric resection. We prefer, and carry out, resections of the stomach when feasible. In the two cases recorded here, however, repeated severe bleeding had so depleted the patients' strength that they were poor operative risks and we feared that subtotal gastrectomy would prove too radical a procedure. Gastroduodenostomy was followed by complete relief for three years in one case and by very satisfactory relief for two years in the other. The second patient still has a high gastric acidity and recently had some heartburn, which was relieved by a few alkaline powders.

TECHNIC

The proper development of gastroduodenostomy technically is entirely dependent on an adequate mobilization of the second and at times even the third part of the duodenum. Unless one has seen or tried mobilization of the second part of the duodenum one has no conception of the ease with which it can be done or of the degree to which the duodenum can be brought up from its bed around the head of the pancreas.

We prefer a retracting incision of good length in the upper part of the right rectus muscle. This permits either gastroduodenostomy or, if need be, any other operation on the stomach. The stomach and colon are retracted and walled out of the field by gauze pads. Other gauze pads are placed over the inferior surface of the liver, which is now retracted. The peritoneum, just lateral to the duodenum, is incised (fig. 2), and since this layer is almost bloodless it can rapidly be freed from the cellular tissue beneath it. The duodenum should be freed well up around the first part and down as far as is necessary to permit it to lie readily against the stomach, the surgeon using care not to be too rough and so cause bleeding in the adjacent pancreatic tissue.

When the duodenum has been adequately freed it is possible to lay it with no tension whatever and with no rotation or twisting of its lumen against the greater curvature of the stomach in the prepyloric area.

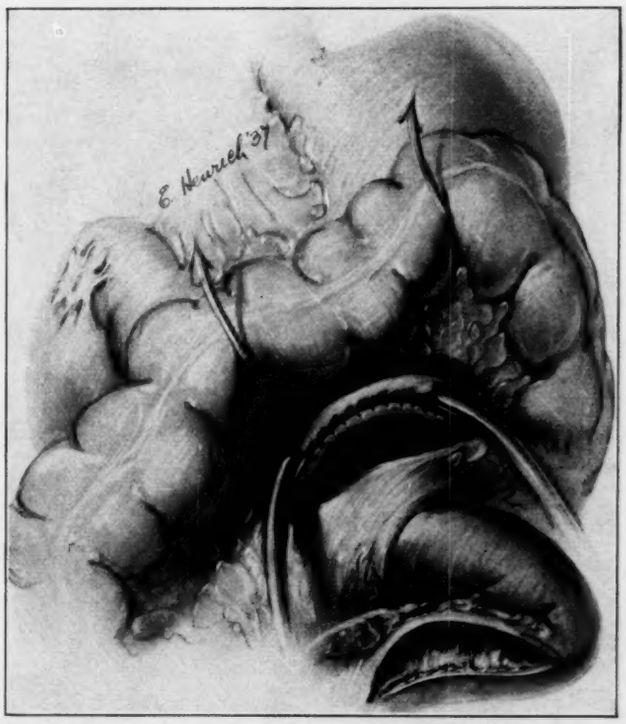


Fig. 8.—The defect in the stomach left after detaching the jejunum has been closed. The jejunum is to be closed next by suturing it transversely.

Figure 3 shows the wrong way to lift up the duodenum. The clamp has been applied to the outer border of the second part of the duodenum, and as this pulls it upward it inevitably must roll the duodenum and so narrow its lumen. Figure 4 shows the correct way to lay the duodenum against the greater curvature of the stomach by placing Allis clamps along its superior border. When the duodenum has been sufficiently mobilized, no obstruction to its lumen results from the procedure.

It is our belief that certain reports in the literature of the occurrence of serious difficulties immediately after gastroduodenostomy, such as persistent vomiting and obstruction, are perhaps related to the fact that the duodenum was rotated when it was laid against the stomach instead of being lifted bodily over to the greater curvature of the stomach.

Figure 5 shows a stay suture placed at the superior end of the duodenum, near the pylorus, and holding forceps bringing the greater curvature of the stomach

and the mesial border of the duodenum together for the placing of the stay suture at the lower end of the anastomosis. Figure 6 shows the posterior layer of sutures, which we always place with fine silk, already finished. The stomach wall has been opened, any bleeding vessels have been caught and tied, the duodenal wall has been opened, and the second layer of sutures, which we make with fine chromic catgut, is just being started.

We do not use clamps for gastroduodenostomy. In the first place it is difficult or impossible to place them,

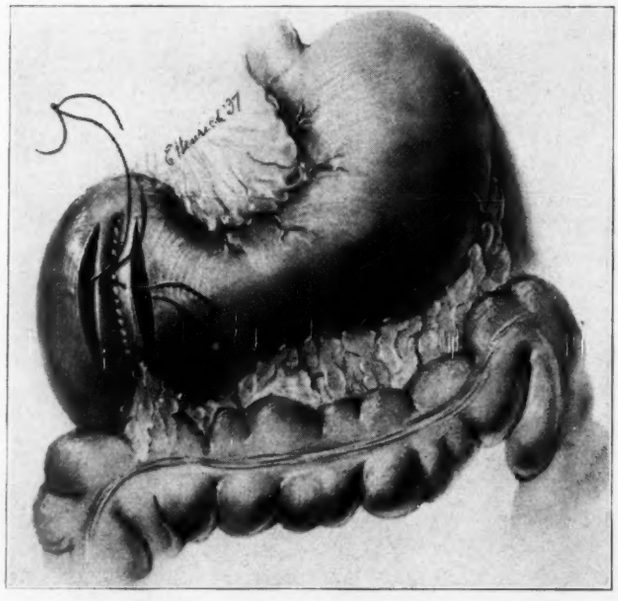


Fig. 9.—The gastroduodenostomy passageway being made after the jejunum has been removed from the stomach and the defect in the greater curvature of the stomach closed. Subtotal gastrectomy added to these preliminary procedures may be too much surgical intervention for the patient. Gastroduodenostomy can be quickly and easily done with much less shock and will overcome pyloric spasm and obstruction.

and in the second place we like to see any bleeding vessels so that we can catch them individually and tie them.

We use the greatest care in walling off the entire abdomen, especially the subphrenic and subhepatic areas, before opening the stomach or duodenum. By the constant use of suction we prevent to a great degree any soiling of the area.

The gastroduodenostomy suturing is now finished, just as in any gastrointestinal anastomosis, and, when the outer layer of silk sutures is completely in place, bits of omentum are brought in and tied over the suture line to make further protection.

Figures 7, 8 and 9 show the use of gastroduodenostomy in the complicated surgical technic necessary for the cure of gastrojejunal ulcers. The jejunum is first separated from the stomach, as shown in figure 8, and the defect in the greater curvature of the stomach is closed by a double layer of sutures. The defect in the jejunum is now closed by suturing the longitudinal hole transversely after the Heinecke-Mikulicz method. In figure 9, one can see the outline of the defect made in the greater curvature of the stomach by closing the opening which was previously anastomosed to the jejunum. One sees also, in this schematic drawing, the first row of sutures placed in the gastroduodenostomy, and one notes the location of the openings in the greater curvature of the stomach and the second part of the duodenum, which are to be joined.

In conclusion, then, we would urge that gastroduodenostomy be given more consideration when surgical treatment is necessary in the management of certain duodenal ulcers. Although opinions and experiences as to the occurrence of stomal ulcers after gastroduodenostomy differ widely, we have been unable to discover evidence of a high percentage of these postoperative complications. We believe that gastroduodenostomy results in a nearer approach to normal gastric physiology than other short-circuiting operations. Our clinical experiences with this operation have been very satisfactory.

171 Bay State Road.

ABSTRACT OF DISCUSSION

DR. ROBERT S. DINSMORE, Cleveland: The authors have called attention to an operative procedure which is not in common use. Obviously this procedure has the advantage that any pyloroplasty does, in that it cannot be followed by a jejunal ulcer and that in most hands it would have a lower mortality rate than gastric resection. Theoretically it should offer the advantage of emptying the gastric secretion into the duodenum rather than the jejunum. Moynihan has cited three types of cases which prevent this operation from having a wide application: first, cases in which there is a large active ulcer of the duodenum accompanied by infection and edema in the surrounding areas; second, cases in which the duodenum is immobile because of chronic adhesions either from a previous ulcer or from disease of the gallbladder, and, third, cases in which there is an obstruction by the third portion of the duodenum as the result of pressure from the superior mesenteric artery or the right or middle colic artery and tuberculous glands. In the United States the incidence of tuberculous glands is low, and from a practical standpoint the third type of case is not as important as the first two. Moynihan also made the point that the convalescence of the patient is not as smooth as after an ordinary gastro-enterostomy. This has not been the experience of Dr. Clute and Dr. Sprague. Cases of the types cited, with the small number of cases of duodenal ulcer which are referred to the surgeon by the gastro-enterologist, leave a limited number to which the operation may be adapted. At the Cleveland Clinic during the past year only 5 per cent of the patients with duodenal ulcer came to the surgeon. I am in accord with the authors when they state that the operative procedure for the cure of a gastrojejunal ulcer may be a formidable task. Immobilization of the ulcer itself in some instances is difficult. In addition there must follow resection of the ulcer, resection of the stomach, closure of the duodenal stump and anastomosis of the jejunum to the stomach. Occasionally the anastomosis has to be made at a site which is not adaptable to the opening in the jejunum, which follows the resection of the ulcer. If possible it would be a great advantage to do the simple procedure which the authors used in their two cases. A striking fact is that in the 400 collected cases there were only three stomal ulcers. This perhaps supplied the greatest argument for the use of this procedure.

DR. HAROLD LINCOLN THOMPSON, Los Angeles: Dr. Clute and Dr. Sprague have made a definite contribution to American experience with gastroduodenostomy. They stated that the operation should be limited to selected cases. All their cases were complicated, and despite the fact that they did not observe a lowering of acidity and their suggestion that subtotal resection might have been preferable in some instances, the clinical results were good. Since Jaboulay first suggested gastroduodenostomy forty-six years ago the operation has not come into general use because of certain technical difficulties and the widespread use of gastrojejunostomy. Gastrojejunal ulcer has brought the latter operation into current and growing disfavor. For this reason the attention of American surgeons has been directed toward plastic or other short-circuiting operations. In continental

Europe subtotal gastric resection is widely used in the treatment of duodenal ulcer. In spite of certain objections this procedure has a firm physiologic basis. The surgeons who have had the greatest experience with gastroduodenostomy are Flint of Leeds and Wilkie of Edinburgh. Flint has used the operation almost exclusively in 200 cases, whereas Wilkie has used it in approximately 160 cases. The critical remarks of Wilkie are noteworthy because he also uses other forms of operation in the treatment of peptic ulcer. He employs the operation for recurrent irritable ulcers with hypersecretion in patients whom he considers unsuitable for gastrojejunostomy. His results do not equal those of gastrojejunostomy. The results were excellent with 64 per cent of his patients, and an additional 25 per cent were relieved but not cured. Stomal ulcer was present in two instances. There is a difference of opinion regarding the effect of gastroduodenostomy on the secretory and motor functions of the stomach. I have conducted extensive studies on the effects of various surgical procedures on these functions. In 1932 I reported the effects of graduated resection of increasing portions of the pylorus in dogs. I observed a reduction in acid values directly proportional to the amount of pylorus removed. At the same time I made observations on gastroduodenostomy. In the gastric contents, after a meat-water test meal or the injection of histamine, the hydrogen ion concentration was not reduced. However, according to fractional analysis the volume of gastric contents is increased and the emptying time of the stomach is prolonged. The amount of bile in the gastric contents also is increased. I have employed gastroduodenostomy in the treatment of twelve patients with complicated peptic ulcer. Despite careful selection of cases, there was one death. Otherwise the clinical results were good.

DR. M. E. STEINBERG, Portland, Ore.: The authors' remarks on the physiology and the anatomic relationships of gastroduodenostomy are in agreement with clinical experience and some experimental evidence. It remains for me to emphasize that an extensive mobilization of the duodenum entails certain dangers. The stomach, filled with bile, pancreatic juice and blood, pulling the duodenum to the left side, may kink it on the mesocolon or the root of the mesentery. Some fatalities due to a high duodenal obstruction have been reported after a Finney-Haberer gastric resection. There is some troublesome retention and vomiting after the Finney-Haberer modification of the Billroth I stomach resection. The mobilization of the duodenum, which is pulled to the left side by the stomach, may also pull or twist the common duct and produce pancreatitis. I have performed eleven gastric resections of the Finney-Haberer type in suitable cases with excellent results. This operation is contraindicated for fat patients because the blood supply on the outside of the duodenum is extensive and the mobilization more difficult. A gastroduodenostomy or a Finney-Haberer resection will not prove successful in the presence of stasis in the duodenum. I have performed 131 stomach resections, with three fatalities. Two of the fatalities were in connection with a secondary operation for jejunal ulcer and only one in connection with a primary resection. I believe that a gastroduodenostomy should give good results in a certain percentage of cases. In view of my experience I must remain satisfied with the resection in preference to any indirect procedure, hoping that the results in the future will be as favorable as they have been in the past.

DR. HOWARD M. CLUTE, Boston: The postoperative obstruction following gastroduodenostomy, to which Dr. Steinberg refers, has been reported frequently in the literature and has been in the past a common and serious complication of the operation. I believe this difficulty is due to rotation of the duodenum as it is laid against the stomach. This we have studiously avoided in our cases, as shown in the artist's drawing. In our experience vomiting after gastroduodenostomy has not been a problem. I do not wish to leave with you the impression that I consider gastroduodenostomy a panacea for all duodenal ulcers and believe that it will replace all other methods of treatment. I do, however, wish to emphasize three situations in which this operation has been helpful to us. 1. Gastroduodenostomy with local anesthesia has been technically easier for me than posterior gastro-enterostomy in treating certain very sick patients with long-standing and severe pyloric obstruction. 2. In certain cases of serious hemorrhage from a duodenal ulcer gastroduodenostomy may be life saving. It may permit vision and suture of the bleeding ulcer as well as relief of the pyloric obstruction. 3. In occasional cases of bleeding gastrojejunal ulcer, gastroduodenostomy can safely replace gastric resection after the gastrojejunal ulcer has been removed. By this lesser procedure the operative shock is lessened and yet the pyloric obstruction and spasm related to the original duodenal ulcer are relieved.

Clinical Notes, Suggestions and New Instruments

DIPHTHERITIC INVOLVEMENT OF THE LIPS, WITH ABSENCE OF SIGNS IN THE NOSE AND THROAT

H. JERRY LAVENDER, M.D., AND JOHN B. SQUIRES, M.D.
CINCINNATI

No mention can be found in the literature of cases in which diphtheria involved the lips and buccal membranes alone, with repeated negative clinical signs in the nose and throat. Believing this to be the first report of such an involvement, we present the following report:

J. M. W., a colored girl aged 10 years, was admitted to the children's burn ward at the Cincinnati General Hospital Oct. 16, 1937, with an extensive (60 per cent total body area) second and third degree burn from fire. The face and neck were spared. She was in deep shock. Intravenous dextrose and a blood transfusion were given immediately, along with other antishock therapy. In view of the extent of the burn, she did well; daily transfusions were given and the burned areas were treated locally with wet dressings of solution of aluminum acetate and green soap tub baths as soon as the patient could tolerate them. Cultures of material from the nose and throat on the second day were negative for Klebs-Loeffler bacilli.

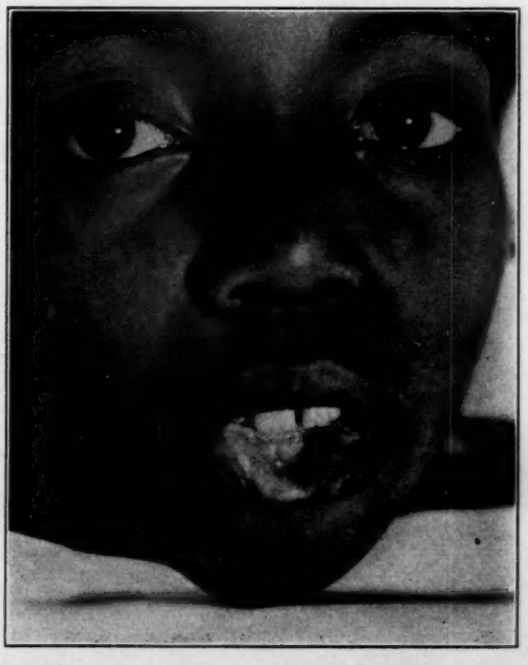


Fig. 1.—Diphtheria of lip, showing ulcerous area seventy-two hours after onset.

At midnight October 27 (the twelfth hospital day) swelling of the lower lip was noted. Eight hours later two thirds of

From the Department of Dermatology and Syphilology, Pediatric Division, Cincinnati General Hospital.

the lower lip was involved in a granular lesion covered with a tough whitish membrane. On the right buccal mucous membrane were similar small round patches. A stained smear (carbol gentian violet) showed many short chained cocci but no fusiform bacilli.

On culture of material from the area, hemolytic streptococci and staphylococci were found. Culture of material from the nose and throat were again negative for Klebs-Loeffler bacilli. Within twelve hours an area in the center of the lower lip 1 cm. in width and 1 cm. in depth began to slough, and sloughing was complete within twenty-four hours. The surface of the ulcer was now smooth and a deep red and involved the entire lower lip. Sulfanilamide was given in 5 grain (0.3 Gm.) doses four times a day. Ten cc. of polyvalent antistreptococcus serum was given intravenously along with 5 minims (0.3 cc.) of epinephrine, 10 cc. of calcium gluconate and 200 cc. of physiologic solution of sodium chloride. The next day another culture of material from the area of the lip was morphologically positive for Klebs-Loeffler bacilli; that from the nose and

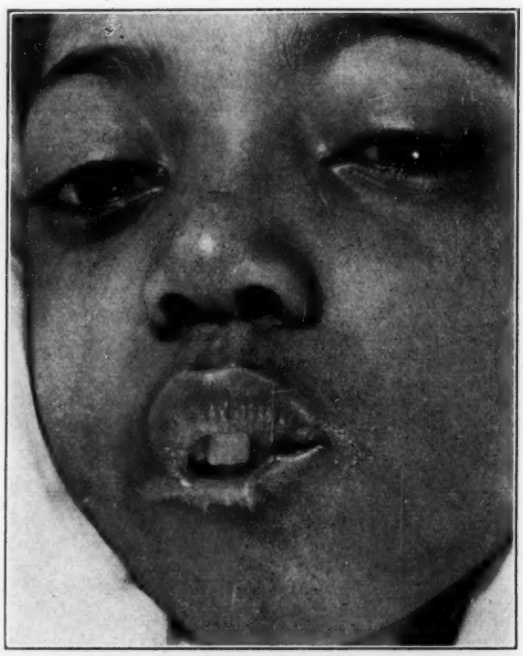


Fig. 2.—Healed upper and lower lips one month after onset.

throat was still negative. The temperature ranged from 99.4 to 101.8 F. Progression of the lesion ceased. On the fifteenth hospital day polyvalent antistreptococcus serum was given as before. Repeated cultures of material from the nose and throat were negative for Klebs-Loeffler bacilli, while cultures from that of the lesion of the lips were positive. On the twenty-first day a virulence test of the organism from the labial lesion was reported positive. At this time the lesion involved the right side of both upper and lower lips and extended onto the lower gums. No ulcerations were seen on the buccal mucous membrane. Careful vaginal examination revealed no ulcers or scars. The white blood cells numbered 34,050 with 60 per cent polymorphonuclear neutrophils and 34 per cent lymphocytes. Diphtheria antitoxin, 10,000 units, was administered intramuscularly. On the twenty-third day a culture of material from the throat was reported positive for Klebs-Loeffler bacilli for the first time and negative for hemolytic streptococci. Cultures from the burned areas were negative for both. The ulceration of the lip was healing somewhat but the process was extending along the lower alveolar ridge. The patient had a spiking type of temperature, but no evidence of pulmonary or renal infection was found. Repeated blood cultures and Kahn reactions were negative. On the thirtieth day two lower incisor teeth became so loose that the patient extracted them herself. Cultures from material in these sockets also showed Klebs-Loeffler bacilli. The lip was healing nicely but ulceration of the gums was more marked. At no time was there any membrane or any clinical evidence of diphtheria in the nose or throat. Diphtheria antitoxin was again given. On the fortieth hospital day the use of a 2 per cent aqueous solution of gentian violet on the gums was begun. Cultures continued to be positive for Klebs-Loeffler bacilli. Within another week, however, the lip and gums were entirely healed and cultures became negative and remained so. Progress was noted in the healing of the burned areas.

The salient points in this case were:

1. Diphtheritic involvement of the lips with ulcerations.
2. Diphtheritic involvement of the buccal membranes.
3. Diphtheritic involvement of the gingival area.
4. Positive virulence test with Klebs-Loeffler bacilli from the lips and buccal membranes.
5. The finding of Klebs-Loeffler bacilli from tooth sockets (alveoli).
6. Consistently negative clinical signs in the nose and throat.
7. Consistently negative cultures for Klebs-Loeffler bacilli in the burned areas.
8. Healing of ulcerous area, and recovery.

717 Provident Bank Building.

AN UNEXPECTED ELECTROCARDIOGRAM OF THE FETUS

ALLEN S. JOHNSON, M.D., SPRINGFIELD, MASS.

Electrocardiograms of the human fetus in utero are apparently comparatively rare; a search through the *Quarterly Cumulative Index Medicus* for the past five years discloses no references in the literature except for the work of Strassmann and his associates [1] in Germany in 1933, which was summarized by Strassmann [2] in this country in 1936. Sachs [3] had reported such studies in 1922, as did some Japanese workers [4] seven years later.

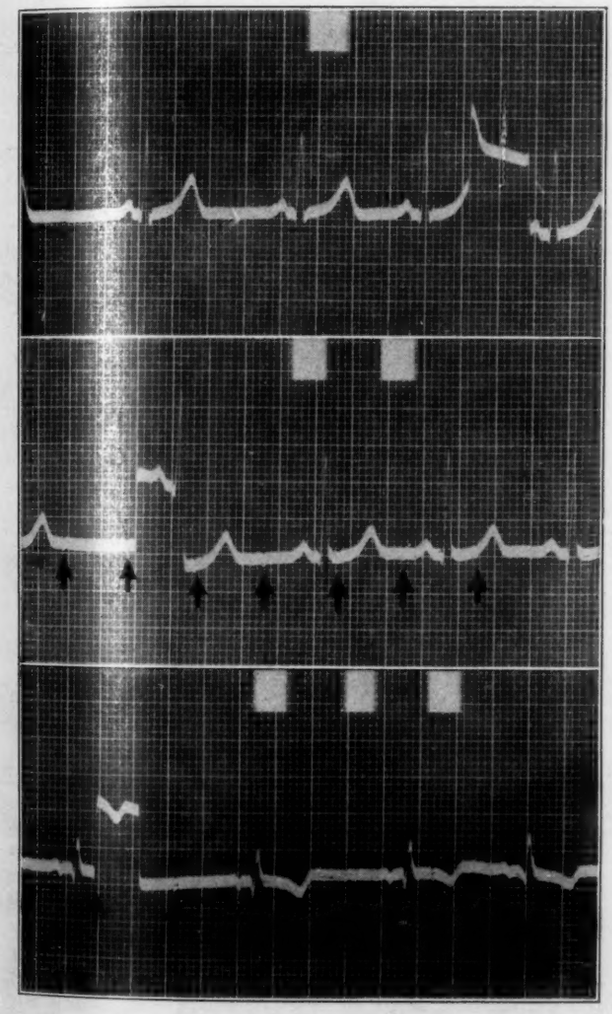
There are two possible explanations for the rarity of such observations in the face of the immense amount of electrocardiographic material now available. The galvanometric deflections of the electrocardiogram of the fetus are so faint that they defy detection unless the base line is smooth and entirely free of oscillations. And even with an ideal graphic background the human fetal heart and the corresponding cardiac current are too weak to appear in a routine electrocardiogram, as Strassmann [2] has pointed out. Nor did the use of a rectal or a vaginal electrode insure satisfactory results. After experimenting on pregnant domestic animals, Steffan and Strassmann [1] evolved a special apparatus and technic which enabled them to secure electrocardiograms of the human fetus late in pregnancy. The reasons for reporting the following case are twofold. Electrocardiograms of the fetus are still something of a medical curiosity; secondly, these tracings, in contrast to the foregoing, were obtained while a routine four lead electrocardiogram on the mother was being taken with an audion tube type of machine (Sanborn cardiette), which is in common clinical use throughout the country.

REPORT OF CASE

Mrs. B. M., a primipara aged 19, almost at term, was referred by Dr. A. F. G. Edgelow because of a pronounced cardiac irregularity of one month's duration. The patient herself was unaware of this arrhythmia and the pregnancy had otherwise been without incident. Clinical examination suggested

1. Steffan, Helmut, and Strassmann, E. O.: Das fetale Elektrokardiogramme, Zentralbl. f. Gynäk. **57**: 610-615 (March 18) 1933.
2. Strassmann, E. O.: The Fetal Electrocardiogram Late in Pregnancy, Proc. Staff Meet., Mayo Clin. **2**: 778 (Dec. 2) 1936.
3. Sachs, H.: Elektrocardiogrammstudienen am Foetus in Utero, Archiv. f. Physiol. **197**: 536, 1922.
4. Maekawa, Magojira, and Toyoshima, Junijira: The Fetal Electrocardiogram of the Human Subject, Acta Scholae med. univ. imp., Kioto **12**: 519, 1930.

a sinus arrhythmia, and an electrocardiogram was taken for confirmation. In the course of routine measurements, regularly recurring negative deflections about 0.5 mm. deep were encountered in leads 2, 3 and 4F (apex and left leg). These may be located by the arrows in the accompanying illustration. They were absent from leads 1 and 4R (apex and right arm) presumably because this electrical axis did not pass sufficiently close to the mother's pelvis to pick up the fetal currents. These fetal electrocardiographic deflections were at first thought to be artefacts, and a well known cardiologist was quite emphatic on this point, though it must be admitted that he was not told of the patient's pregnancy when the tracings were submitted. The true nature of these minute deflections became



The arrows point to the fetal deflections.

apparent when it was found that their frequency corresponded to the fetal heart rate. This opinion was subsequently confirmed by Drs. Paul D. White and Burton Hamilton of Boston.

In contrast to the tracings published by Strassmann,[2] the electrocardiogram in the present case showed slight changes in the fetal heart rate in lead 2. The patient was delivered of a normal full term child thirteen days later, but at the time of discharge from the hospital she still showed a marked sinus arrhythmia.

In the illustration unfortunately it is almost impossible to identify the fetal cardiac deflections even though they are located by means of arrows. Some of them may be detected by means of a 5 power lens and the rest must be taken on faith although they were quite obvious to the naked eye on the original tracings.

121 Chestnut Street.

A CASE OF CHIARI'S NETWORK ASSOCIATED WITH A MURMUR RESEMBLING THE BRUIT DE ROGER

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This singular cardiac anomaly was first described in 1897 by Chiari,[1] who reported a series of eleven cases in which he found a peculiar network of fibers occupying the right auricle. This network he considered a developmental anomaly consisting of an incomplete residuum of the valvula venosa dextra and the septum spurium, which are represented only by threads attached to the eustachian and thebesian valves on the one side and to the crista terminalis or to the region of the tuberculum loweri on the other. The published reports would seem to indicate that the anomaly is very rare, although Yater[2] estimates that it occurs in from 2 to 3 per cent of hearts which are otherwise normal developmentally and Helwig[3] concludes that such reticula are "found to be present in 1.5 per cent of routine autopsy examinations." Probably it would be found more frequently if it were systematically looked for. Yater,[2] who has discussed the abnormality fully, collected from the literature twenty-five cases in addition to those reported by Chiari, four of which he himself had described, and reported still another case of his own. In no instance had the diagnosis been made prior to death, and in only one case had any physical signs been observed which might be attributed to the network. This case was reported by Alvarez and Herrmann[4] in 1931. These authors noted a "most peculiar low pitched thonging murmur heard along the right sternal border from the third rib region downward," which had a musical quality "and faded off into a distant purr." It resembled the venous souffle which is heard at times over the jugular bulb. The diastolic murmur of aortic regurgitation and a characteristic Austin Flint murmur were also heard. Some doubt has been expressed as to whether the murmur in this case actually was produced by the network, as assumed by Alvarez and Herrmann, since there were other more common pathologic conditions present. The general opinion is that the network produces no symptoms or signs and is of interest clinically only as affording an occasional source of pulmonary embolism.

The following typical case of this congenital defect came under my observation in May 1937 and is of especial interest because of the presence of a murmur almost identical with that described by Alvarez and Herrmann, which suggests the probability that the network at times may give rise to an auscultatory sign.

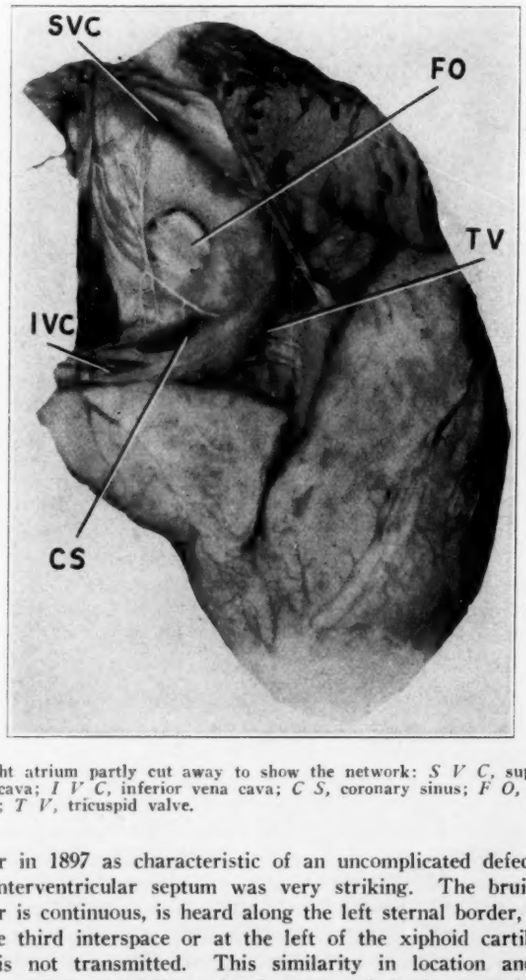
REPORT OF CASE

J. M., a Negro fisherman, aged 40, was admitted to the medical floor of the Roper Hospital May 3, 1937, five days after his discharge from the surgical floor, where he had been treated for extravasation of urine. His previous history included syphilis and gonorrhea, and at the age of 30 he had an illness characterized by migratory arthritis. There was no history of previous heart disease. The diagnosis on admission was pneumonia. On physical examination fine rales were heard scattered over the right side of the chest anteriorly, in the left axilla and in the left side of the chest posteriorly from the third to the sixth rib. The blood pressure was 220 systolic, 130 diastolic; the arteries were thickened. The heart was enlarged and a systolic murmur at the apex transmitted to the left axilla and gallop rhythm were noted. The chief interest was centered on a continuous humming murmur with systolic accentuation at the sternal end of the fourth and fifth left interspaces, which resembled the so-called venous hum. The area of distribution was quite limited, the murmur fading away as the stethoscope approached the apex, the aortic or the pulmonary valve region.

1. Chiari, Hans: Netzbildungen im rechten Vorhofe des Herzens, Beitr. z. path. Anat. u. z. allg. Path. **22**:1, 1897.
2. Yater, W. M.: The Paradox of Chiari's Network, Am. Heart J. **11**:542 (May) 1936.
3. Helwig, F. C.: The Frequency of Anomalous Reticula in the Right Atrium of the Human Heart "Chiari Network": Report of Eight Cases, Am. J. Path. **8**:73 (Jan.) 1932.
4. Alvarez, J. A., and Herrmann, G. W.: Unusual Signs from an Expansive Chiari Network Along with Signs of a Syphilitic Aortic Regurgitation, Am. J. Syph. **15**:532 (Oct.) 1931.

The urine was of normal specific gravity and contained a small amount of albumin and occasional granular casts. The blood showed sickle cells but nothing else of significance. Kolmer and Kline tests were negative. The complement fixation test for gonococcic infection was markedly positive. Urea nitrogen was 150 mg. per hundred cubic centimeters of blood, and creatinine 9.6 mg. per hundred cubic centimeters. An electrocardiogram showed normal axis, depressed S-T interval in leads 2 and 3, and apparent inversion of T_3. The eyegrounds showed sclerosed arteries, numerous areas of retinal degeneration, probably the result of old hemorrhages, and one or two recent hemorrhages in both fundi. A roentgenogram indicated moderate general enlargement of the heart and generalized increase in bronchovesicular markings throughout both lungs.

This was clearly a case of hypertensive cardiovascular disease with uremia and bronchopneumonia. The unusual murmur was difficult to explain and occasioned much discussion and difference of opinion. Its resemblance to the murmur described by



Right atrium partly cut away to show the network: *S V C*, superior vena cava; *I V C*, inferior vena cava; *C S*, coronary sinus; *F O*, fossa ovalis; *T V*, tricuspid valve.

Roger in 1897 as characteristic of an uncomplicated defect of the interventricular septum was very striking. The bruit de Roger is continuous, is heard along the left sternal border, best at the third interspace or at the left of the xiphoid cartilage, and is not transmitted. This similarity in location and in character led to the diagnosis of patency of the interventricular septum.

The pathologic diagnosis after autopsy was hypertensive cardiovascular disease with arterial nephrosclerosis, and lobular pneumonia as a terminal event. When the heart was opened a characteristic network of fibers was found in the right auricle with no septal or valvular defect.

The following description of the heart is given by Dr. T. M. Peery, who performed the autopsy:

The heart was greatly enlarged, weighing 575 Gm. Its epicardial surface was smooth and glistening. On section the myocardium of the left ventricle averaged about 1.6 cm. in thickness; that of the right ventricle about 2 to 4 mm. All the valves appeared normal. The aortic ring measured 7.3 cm. in circumference, the mitral 10 cm., the pulmonary 9 cm. and the tricuspid 12 cm. In the right atrium was a network of fibers, the central portion of which lay free in the orifice of the inferior vena cava and the cavity of the atrium. The total length of the network varied from 5 to 8 cm. Its upper and anterior attachment extended in a more or less straight line, 3 cm. in length, from the right border of the superior vena cava, just below and behind the lower margin of the crista terminalis, downward along the right wall of the atrium to a point about 5 mm. above the entrance of the inferior vena cava. At its attachment to the atrial wall it was a fenestrated membrane, roughly triangular, with numerous large defects, from the apex of which, and from its inferior border, numerous slender bands arose, which branched and joined other bands in an irregular fashion. The opposite attachment of the network extended linearly from the right margin of the inferior vena cava, upward and to the left, following the limbus of the inferior vena cava for about 2.5 cm., and then crossed the open mouth of the coronary sinus, which in this case had no other valve protecting it. At its left margin the membrane was triangular, measuring 1 cm. at its base and about 6 mm. in height, and was not fenestrated. From the apex the fibers converged, branching and joining other branches as at the other attachment. The fibers arising from the upper end of the right line passed to the lower end of the left, and those from the lower end of the right to the upper end of the left, so that as the membrane was stretched it appeared to be slightly twisted on itself. At the center of the network it was composed of from five to eight intercommunicating fibers of about the thickness of a slender chorda tendinea, as shown in the accompanying illustration. The foramen ovale can be entered by a flat probe, although it was at such an angle and so well protected by flaps on both the right and left atrial surfaces that it was probably not functionally open. The interventricular septum was intact, although the membranous portion of the septum was thin and transparent. The ductus arteriosus was closed. No other congenital abnormality of the heart was noted. The coronary arteries were patent but showed small atheromatous plaques.

COMMENT

The only importance that has been attached to Chiari's network is the possibility of its affording a site for thrombus formation, which may become the source of a pulmonary embolus, as in the case reported by Ebbinghaus.[5] No physical signs have been noted except by Alvarez and Herrmann. In the case reported here there was no abnormality of the heart other than a partial patency of the foramen ovale, which was functionally closed, and it is very improbable that the murmur which was heard could be produced by the foramen ovale under such conditions. In the absence of patency of the ductus arteriosus or of any other defect it seems reasonable to conclude that the continuous murmur heard actually was produced by the network. The similarity between the murmur in this case and the murmur described by Alvarez and Herrmann is very striking, and since the network was the only point of identity in the pathologic changes observed in the two cases the assumption that it produced the murmur in both would appear warranted. That no murmur was observed when the patient was under treatment in the surgical ward possibly may be explained by its limited area of distribution and its situation. In a routine examination to determine the presence of valvular defects it might easily be overlooked, as it was not heard at any of the valve areas. Furthermore, it varied in distinctness so that at times it was heard with difficulty. The resemblance of the murmur to the bruit de Roger is so close that the differentiation of the two would be difficult or impossible.

CONCLUSION

A continuous murmur occupying the site of the murmur reported here may be a sign of Chiari's network as well as of patency of the interventricular septum.

5. Ebbinghaus, H.: Zur Kasuistic der kongenitalen Herzfehler und deren möglichen Folgen, München. med. Wchnschr. **51**: 797, 1904.

The Chemical Laboratory

IN THE JOURNAL, NOV. 6, 1937, THERE APPEARED, UNDER THE AUSPICES OF THE A. M. A. CHEMICAL LABORATORY, A NUMBER OF REPORTS DEALING WITH ELIXIR OF SULFANILAMIDE-MASSENGILL. TWO OF THESE WERE ENTITLED "PRELIMINARY REPORT OF TOXICITY STUDIES ON RATS, RABBITS AND DOGS (FOLLOWING INGESTION IN DIVIDED DOSES OF DIETHYLENE GLYCOL, ELIXIR OF SULFANILAMIDE-MASSENGILL AND 'SYNTHETIC' ELIXIR)," BY DR. E. M. K. GEILING, JULIUS M. COON AND DR. E. W. SCHOEFFEL, AND "PATHOLOGIC EFFECTS FOLLOWING THE INGESTION OF DIETHYLENE GLYCOL, ELIXIR OF SULFANILAMIDE-MASSENGILL, 'SYNTHETIC' ELIXIR OF SULFANILAMIDE AND SULFANILAMIDE ALONE" BY DR. PAUL R. CANNON. IN THE EARLY COMMUNICATIONS IT WAS STATED THAT DRS. GEILING AND CANNON WOULD MAKE FURTHER STUDIES. THESE ARE REPRODUCED HEREWITH UNDER THE AUSPICES OF THE A. M. A. CHEMICAL LABORATORY.

PAUL NICHOLAS LEECH, Director,
A. M. A. Chemical Laboratory.

PATHOLOGIC EFFECTS OF ELIXIR OF SULFANILAMIDE (DIETHYLENE GLYCOL) POISONING

A CLINICAL AND EXPERIMENTAL CORRELATION: FINAL REPORT

E. M. K. GEILING, M.D.
AND
PAUL R. CANNON, M.D.
CHICAGO

During the months of September and October 1937 at least seventy-six [1] human beings in various localities died as a result of poisoning by Elixir of Sulfanilamide-Massengill.[2] By analysis,[3] the A. M. A. Chemical Laboratory found this preparation to be essentially a 10 per cent solution of sulfanilamide in about 72 per cent diethylene glycol, together with some coloring and flavoring agents. There were no contaminants such as mercury, the effects of which might have resembled the clinical symptoms produced by the elixir. Apparently the makers of this product were unaware of its possible toxicity and distributed it freely without having tested it adequately on animals. It had not been submitted to the Council on Pharmacy and Chemistry of the American Medical Association nor did the Food and Drug Administration of the United States Department of Agriculture know of its composition. Newspaper reports of deaths from this "new medicine" created consternation among many physicians who were using sulfanilamide. Hundreds of inquiries were received by the American Medical Association asking for information as to the nature of the causative agent and its possible antidote. To answer these pressing queries, experiments [4] were immediately undertaken by us at the request of the A. M. A. Chemical Laboratory. The elixir, its active components (pure diethylene glycol and sulfanilamide) and a "synthetic" composite were tested separately on groups of animals. Rats, rabbits and dogs were given the various drugs three times daily in graded doses. The experiments were devised with the object of developing conditions which might simulate those in the human cases.

From the Departments of Pharmacology and of Pathology, the University of Chicago.

The funds for the experimental work were supplied by the A. M. A. Chemical Laboratory and by a grant from the Committee on Therapeutic Research of the Council of Pharmacy and Chemistry of the American Medical Association.

1. Several sources indicate that the number of deaths was more than 100. The figure quoted here represents the number of confirmed deaths.
2. Elixir of Sulfanilamide-Massengill: II, editorial, J. A. M. A. **109**: 1724 (Nov. 20) 1937.
3. Schoeffel, E. W.; Kreider, H. R., and Petersen, J. B.: Chemical Examination of Elixir of Sulfanilamide-Massengill, J. A. M. A. **109**: 1532 (Nov. 6) 1937.
4. Geiling, E. M. K.; Coon, J. M., and Schoeffel, E. W.: Preliminary Report of Toxicity Studies on Rats, Rabbits and Dogs, J. A. M. A. **109**: 1532 (Nov. 6) 1937.

REVIEW OF THE LITERATURE PRIOR TO THE "ELIXIR" EPISODE

There were in the literature reports dealing with the toxicity of diethylene glycol by Von Oettingen and Jirouch [5] and by Haag and Ambrose.[6] The first named authors studied the acute toxicity of the compound and noted hydropic degeneration of the kidney. Haag and Ambrose, in addition to observing the acute toxicity in rats, also studied the chronic effects of adding it to the drinking water. They found that concentrations of from 3 per cent to 10 per cent proved rapidly fatal. Lower concentrations (0.03 per cent to 1.0 per cent) did not significantly affect the growth of their animals, which were killed and examined after 100 days of observation; no liver or kidney damage was observed. No pathologic changes, apparently, were reported at autopsy on those dying of large doses of diethylene glycol. Although not directly stated in these papers, it would appear that Von Oettingen and Jirouch studied this compound from the point of view of its industrial hazard, and Haag and Ambrose appear to have investigated the compound with respect to its safety as a hygroscopic agent in cigarets. The lack of more complete data concerning the chronic effects of diethylene glycol should have made it even more imperative that it should not have been used as a solvent in therapeutic preparations intended for repeated use in relatively large amounts until additional information concerning its chronic toxicity and fate in the animal body had been secured.

Barber [7] in 1934 reported five deaths from poisoning in factory workers exposed to dioxane, the anhydride of diethylene glycol (diethylene dioxide). At autopsy extensive hemorrhagic nephritis and necrosis of the central part of the liver were observed. The absence of fatty change in the liver in the fatal cases is of particular interest, since such changes do occur with other known poisoning agents on the liver, such as alcohol and chloroform.

In 1935 de Navasquez [8] reported tubular necrosis of the kidneys accompanied by hepatic changes due to experimental dioxane poisoning.

When the "elixir" episode occurred there were also no experiments recorded in the literature dealing with the chronic toxic effects of sulfanilamide. In fact, in a later detailed account of the toxicity of sulfanilamide in animals, Marshall, Cutting and Emerson [9] stated: "Despite the widespread use of sulfanilamide in the treatment of certain bacterial infections, very scanty data are available concerning its toxicity for animals. Several observers have reported on its toxicity, using very limited numbers of animals." However, the available data indicate that sulfanilamide is relatively nontoxic for animals. Furthermore, under the experimental conditions recorded there were no marked renal and

5. Von Oettingen, W. F., and Jirouch, E. A.: Pharmacology of Ethylene Glycol and Some of Its Derivatives, J. Pharmacol. & Exper. Therap. **42**: 355 (Aug.) 1931.
6. Haag, H. B., and Ambrose, A. M.: Studies on the Physiological Effect of Diethylene Glycol, J. Pharmacol. & Exper. Therap. **59**: 93 (Jan.) 1937.
7. Barber, Hugh: Hemorrhagic Nephritis and Necrosis of the Liver from Dioxan Poisoning, Guy's Hosp. Rep. **84**: 267 (July) 1934.
8. de Navasquez, S.: Experimental Tubular Necrosis of the Kidneys Accompanied by Liver Changes Due to Dioxan Poisoning, J. Hyg. **35**: 540-548 (Dec.) 1935.
9. Marshall, E. K., Jr.; Cutting, W. C., and Emerson, Kendall, Jr.: The Toxicity of Sulfanilamide, J. A. M. A. **110**: 252 (Jan. 22) 1938.

hepatic lesions produced by this drug. It may also be emphasized that extensive use in human beings indicate that, when properly employed, it is reasonably safe.

LITERATURE FOLLOWING THE EPISODE

Simultaneously with the publication of our studies on the toxicity of the elixir and its components, there

Fig. 1 (case 9).—Section of the kidney showing focal cortical infarction with peripheral hemorrhage. Reduced from a photomicrograph with a magnification of 16 diameters.

appeared two independent reports on the toxic effects of diethylene glycol. Kesten, Mulinos and Pomerantz [10] reported that diethylene glycol administered to rats by mouth and to rabbits intravenously caused severe injury to the epithelium of the renal convoluted tubules, accompanied by anuria and uremic coma. The liver and adrenals were less regularly involved. Three per cent diethylene glycol (0.9 cc. per rat daily) in the drinking water killed about 50 per cent of the rats within two months; 5 per cent killed 25 per cent within a week. Rabbits were given single injections intravenously. Some animals died and others were killed at varying periods after injection. Significant pathologic lesions were observed in the kidneys of about half of the experimental animals. Holck [11] also reported experiments on rats given diethylene glycol in food and water. A 5 per cent solution of diethylene glycol in the drinking water killed his rats in about eight days, but the pathologic results were inconclusive.

ANIMAL EXPERIMENTS

Our toxicity experiments were undertaken on normal rats, rabbits and dogs. The animals had free access to food and water. In our experiments were used (1) pure diethylene glycol, (2) pure sulfanilamide, (3) Elixir of Sulfanilamide-Massengill and (4) "Synthetic" elixir of sulfanilamide compounded by the A. M. A. Chemical Laboratory with pure substances in approximately the same proportions as found in the Massengill elixir.

Appropriate chemical tests ruled out the possible presence of mercury and of impurities present in the Massengill preparations.

The animal experiments were devised (1) to determine the toxic and lethal doses of each of the substances when given in relatively small doses by stomach tube three times a day. This information seemed particularly necessary since no data on this point were available in the literature; (2) to reproduce in healthy experimental animals in about the same period of time, the clinical and pathologic picture as presented in patients who had taken fatal doses of the Elixir of Sulfanilamide.

There is considerable species, as well as individual, variation in the toxicity of the drugs used under the conditions of our experiments. Rabbits were found to be the most sensitive experimental subjects. The doses used in our first experiments were larger than the amounts that proved fatal to the human beings, which were based on weight relationships. However, in later experiments carried out by Mr. A. Rodaniche on rabbits, doses comparable to the human doses proved fatal in about 30 per cent of the animals. This point is illustrated in table 1. These data are representative of more than fifty such experiments conducted over a similar range of dosages. The wide variations in susceptibility are evident from the table. Data with other species are published elsewhere.[4]

The course of the intoxication in the animals was noted frequently. A toxic syndrome [4] developed which simulated closely the average clinical picture in the human fatal cases; this is described later. In rats, after about the fourth dose, the fur became ruffled, there was increased thirst and some diuresis, food was refused, urinary excretion later became scanty, and eventually complete anuria developed. The animals exhibited an

Fig. 2 (case 11).—Section of the kidney showing diffuse cortical infarction with recent hemorrhage. Reduced from a photomicrograph with a magnification of 17 diameters.

increased rate and depth of respiration and finally died in coma. Rabbits exhibited essentially the same picture but were more sensitive than rats. Dogs too behaved similarly, but the dosage could not be so accurately determined because of the tendency of the dogs to vomit after the administration of both diethylene glycol and the elixirs.

10. Kesten, H. D.; Mulinos, M. G., and Pomerantz, Leo: Renal Lesions Due to Diethylene Glycol, J. A. M. A. **109**: 1509 (Nov. 6) 1937.
11. Holck, H. G. O.: Glycerin, Ethylene Glycol, Propylene Glycol and Diethylene Glycol, J. A. M. A. **109**: 1517 (Nov. 6) 1937.

CONCLUSIONS FROM ANIMAL EXPERIMENTS

Based on more than 100 necropsies and a considerably larger number of experiments, the following summation and conclusions seem warranted:

1. Diethylene glycol was the chief toxic component of Elixir of Sulfanilamide-Massengill examined, because experimental animals given diethylene glycol alone exhibited essentially the same clinical course and pathologic changes in the kidney and liver[12] as did those treated with similar doses of Elixir of Sulfanilamide-Massengill or a "synthetic" elixir containing the ingredients in the same proportion as found by analysis in the Massengill preparation.

2. Sulfanilamide alone, if given in doses of 0.2 Gm. per kilogram three times a day, did not prove fatal to rats, rabbits or dogs after eight or more divided doses. However, when sulfanilamide was given in this dosage in the form of Elixir of Sulfanilamide-Massengill or in the "synthetic" elixir, either preparation was fatal to experimental animals and they presented a clinical and

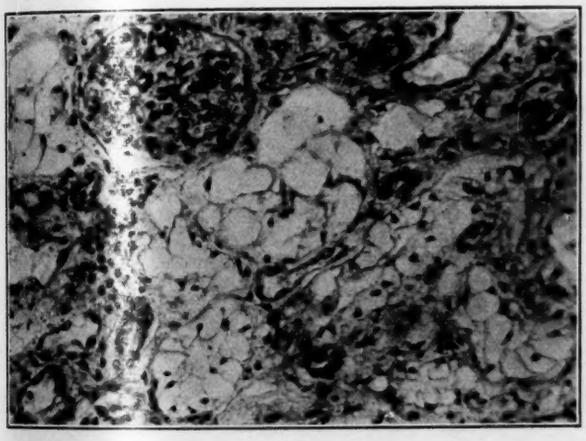


Fig. 3 (case 2).—Section from the kidney. Note the extensive hydropic degeneration of tubular epithelium with obliteration of lumens, the normal glomerulus and the absence of leukocytic infiltration. Reduced from a photomicrograph with a magnification of 360 diameters.

pathologic picture closely resembling that reported for the human cases in which death occurred after ingestion of the Massengill elixir.

3. Although animals receiving sulfanilamide in doses of 0.2 Gm. per kilogram three times a day did not succumb, several of them had convulsions. Numerous animals were killed after having received eight or more divided doses of the drug. None of them had anuria, nor did they exhibit the renal and hepatic changes found in animals treated with either the Massengill or the "synthetic" elixir. While we do not believe that the sulfanilamide had any important part in the intoxications resulting from the elixir of sulfanilamide, one must not overlook the possible damage to tissues that may result when sulfanilamide is administered to experimental animals or to human beings with impaired renal function.[13]

4. The pathologic picture was essentially similar in the three species of animals, whether given the Elixir of Sulfanilamide-Massengill, the "synthetic" elixir of sulfanilamide or diethylene glycol alone. The pathologic changes were those of a severe chemical nephrosis with intracellular edema of most of the epithelial cells of the convoluted tubules, resulting in tubular obstruction by compression and by the intraluminal formation of casts. This intracellular edema in the kidneys leads to internal disorientation of cells of the convoluted tubules and offers an explanation for the tubular obstruction,

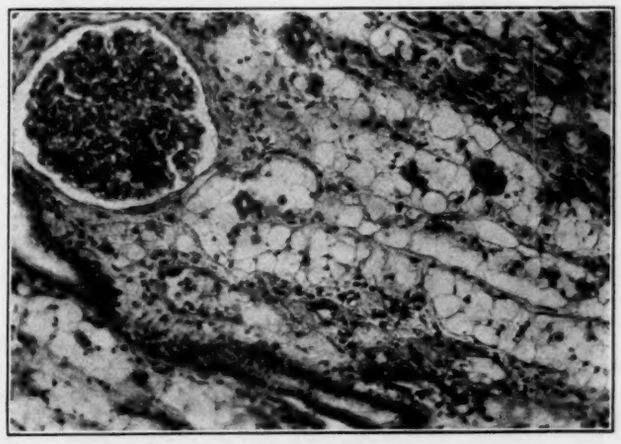


Fig. 4 (case 9).—Section of the kidney showing the severe hydropic degeneration, the normal glomerulus and the absence of leukocytic infiltration. Reduced from a photomicrograph with a magnification of 225 diameters.

anuria, uremia and death. Whether this intracellular change is due to cellular anoxia, with consequent intracellular edema, necrosis and cellular desquamation, or whether it is due to hygroscopic properties of diethylene glycol is a question that must await further investigation.

These changes in the kidneys and liver were not due to sulfanilamide. With sulfanilamide, the microscopic changes were slight and consisted of moderate fatty degeneration in some of the collecting tubules in the dogs and to a lesser degree in the rats. The livers of both dogs and rats showed no hydropic degeneration and practically no fatty degeneration. There is but little question therefore that the severe chemical nephrosis

Fig. 5 (case 6).—Section of the kidney showing focal hydropic degeneration and obliteration of lumens. Reduced from a photomicrograph with a magnification of 360 diameters.

of the dogs, rats and rabbits is due to diethylene glycol alone. We cannot say, however, that under conditions of anuria, with retention of sulfanilamide in the blood stream, some tissue damage by sulfanilamide may not be added to that of diethylene glycol.

12. Cannon, P. R.: Pathologic Effects Following the Ingestion of Diethylene Glycol, Elixir of Sulfanilamide-Massengill, Synthetic Elixir of Sulfanilamide and Sulfanilamide Alone, J. A. M. A. **109**: 1536 (Nov. 6) 1937.

13. Marshall, E. K., Jr.; Kendall, Emerson, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, J. A. M. A. **108**: 953 (March 20) 1937.

COMPOSITE CLINICAL PICTURE IN FATAL HUMAN CASES

The following is a composite clinical picture observed in patients who died following the ingestion of variable amounts of Elixir of Sulfanilamide. The symptoms observed are taken from reports published by Homer A. Ruprecht and I. A. Nelson of Tulsa,[14] by O. E. Hagebusch[15] and by K. M. Lynch,[16] and also from communications by physicians to Dr. Paul N. Leech, Secretary of the Council on Pharmacy and Chemistry of the American Medical Association, and from reports obtained by inspectors of the Federal Food and Drug Administration. The patients ranged in age from 11 months to 70 years; the dosage of Elixir of Sulfanilamide administered ranged from 1½ to 6 ounces (45 to 180 cc.).

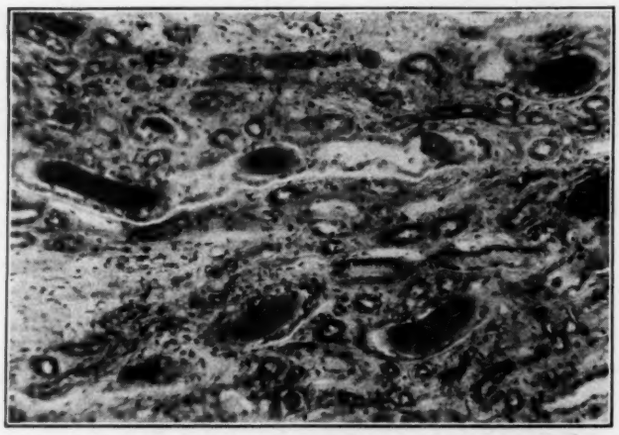


Fig. 6 (case 4).—Section showing hyaline casts in the lumens of the collecting tubules. Reduced from a photomicrograph with a magnification of 225 diameters.

The onset of symptoms was variable; in one instance the patient complained of symptoms immediately after the first dose. Patients usually complained first of a sensation of "heartburn," followed by nausea, abdominal cramps, dizziness, malaise and vomiting, with diarrhea occasionally and later pain in the back over the region of the kidney and in the abdomen. In fact, the condition was thought by some physicians to be an acute abdominal process and surgical intervention was recommended, although this was not carried out. These symptoms occurred about twenty-four hours after medication was started and were followed by oliguria and later anuria. The patients became drowsy and had slight puffiness of the face and slight jaundice in some instances. They became progressively comatose and died in from two to seven days after onset of anuria in uremic coma. The characteristic physical and clinical conditions were cutaneous pallor without cyanosis, slow and deep respirations and varying degrees of pulmonary edema, as manifested by rales throughout both lungs. There were subnormal temperatures and slow pulse, tenderness over the kidneys and upper part of the abdomen and edema of the dependent parts with ascites. The blood pressure was not significantly elevated. There was no anemia, but there was usually a moderate leukocytosis. The urine was scanty and contained four plus albumin, casts and occasional leukocytes.[16a] The nonprotein nitrogen of the blood rose to as high as 200 mg. and the creatinine went up in some patients to 12 mg. per hundred cubic centimeters.

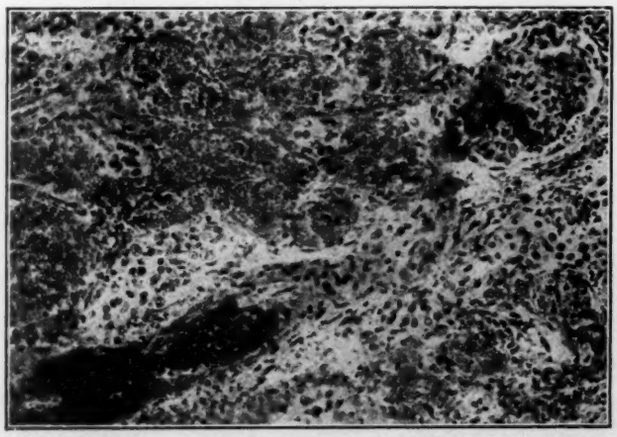


Fig. 7 (case 11).—Section of the kidney showing hyaline necrosis of the blood vessel walls and hyaline thrombosis in the area of recent infarction of the cortex. Reduced from a photomicrograph with a magnification of 260 diameters.

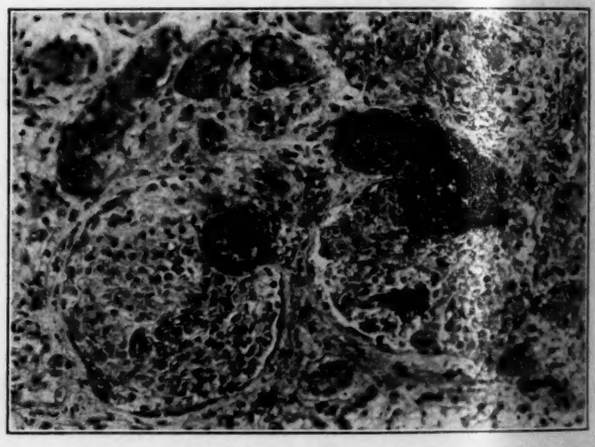


Fig. 8 (case 1).—Section of the kidney showing hyaline necrosis of the vascular walls of afferent glomerular vessels in a region of cortical infarction. Reduced from a photomicrograph with a magnification of 260 diameters.

It may also be stated in passing that there is considerable variation in responsiveness of patients to the elixir. At least 100 persons took doses of the elixir varying from 1 to 8 ounces (30 to 240 cc.) without serious effects, although some did complain of gastric disturbances.

PATHOLOGIC CHANGES IN HUMAN CASES

Of the seventy-six persons who died as a result of ingestion of Elixir of Sulfanilamide, we have been able to examine the tissues from fifteen, and this report deals particularly with twelve of these. The necropsy material was sent to us through the aid of or by federal inspectors of the Food and Drug Administration of the U. S. Department of Agriculture, by the secretary of the Council on Pharmacy and Chemistry of the American Medical Association and by several pathologists who performed the necropsies.[17]

14. Ruprecht, H. A., and Nelson, I. A.: Clinical and Pathological Observations, J. A. M. A. **109**: 1537 (Nov. 6) 1937.

15. Hagebusch, O. E.: Necropsies of Four Patients Following Administration of Elixir of Sulfanilamide-Massengill, J. A. M. A. **109**: 1537 (Nov. 6) 1937.

16. Lynch, K. M.: Diethylene Glycol Poisoning in the Human, South. M. J. **31**: 134-137 (Feb.) 1938.

16a. Similar changes are found in dogs poisoned with diethylene glycol (unpublished data).

17. The following pathologists, who were generous in their cooperation, supplied us with the material for the present study: Dr. Omer E. Hagebusch, St. Louis (cases 1, 2, 3, 4, 5), Dr. Ralph Monger, Knoxville, Tenn. (cases 6, 7), Dr. K. M. Lynch, Charleston, S. C. (cases 8, 9, 10), Dr. R. L. Thompson, St. Louis (case 11) and Dr. Paul Brindley, Galveston, Texas (case 12).

Table 2 is a brief and incomplete summary of the cases reviewed by us and includes the clinical diagnosis, amounts of elixir of sulfanilamide administered, the age of the patient and the like. Three of these have been reported elsewhere (cases 8, 9 and 10) and case 12 is to be reported by Drs. Brindley and Kelsey in a future issue of the *Texas State Journal of Medicine*. We shall attempt, therefore, only to summarize the necropsy results as given in the literature and as obtained from the necropsy protocols and material sent to us for study. Incompleteness of data is due to the fact that many of the necropsies were performed under unfavorable circumstances for weighing organs or because of limitation of permits for necropsy, but in all instances the liver and spleen were carefully examined grossly and microscopically.

In the original telegraphic report sent to the headquarters office of the American Medical Association on Oct. 15, 1937, by Drs. Homer A. Ruprecht and I. A. Nelson,[14] describing the postmortem observations in five cases of poisoning by Elixir of Sulfanilamide at Tulsa, Okla., the following features were mentioned: a tawny but not enlarged liver; kidneys mottled and purple, in severe cases showing superficial cortical necrosis;

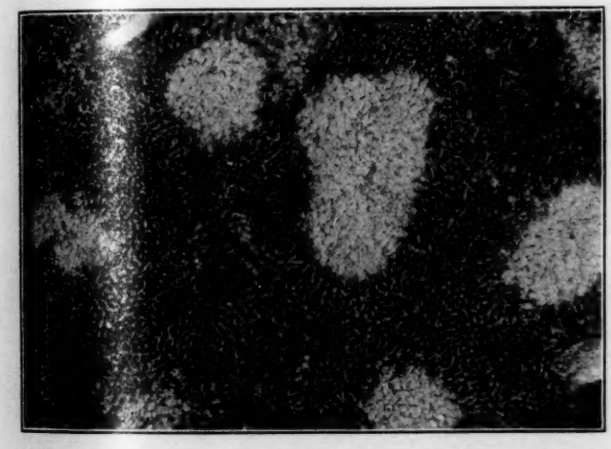


Fig. 9 (case 6).—Section of the 900 Gm. liver showing focal central hydropic degeneration of hepatic cells with absence of marked inflammatory reaction or of actual necrosis. Reduced from a photomicrograph with a magnification of 60 diameters.

pathologic changes in the other viscera insignificant, and inconstant accumulations of clear, straw-colored fluid in the peritoneal, pleural and pericardial cavities. Microscopic examination showed "a consistent hydropic tubular nephrosis with central degeneration of liver with cells showing foamy cytoplasm."

A few days later, Dr. O. E. Hagebusch[15] reported to the A. M. A. headquarters the results of necropsies in four cases at East St. Louis, Ill., as follows: "pulmonary edema, marked nephritis with hemorrhage into the cortex of the kidney, marked hemorrhage into the pericardium, mucosa of the stomach and duodenum and into the serous surfaces of lung and liver. The liver is pale, edematous and enlarged." At about the same time two patients died in Memphis, Tenn., after ingestion of the elixir and the postmortem examinations by Dr. Harry C. Schmeisser, T. C. Moss and C. E. Gillespie revealed a similar picture. Finally, early in October, four persons died in Charleston, S. C., after ingestion of the elixir and necropsies by Dr. K. M. Lynch[16] revealed the general observations just described.

All these observers recognized the unusual nature of the pathologic changes, and both Ruprecht and Nelson, and Schmeisser, Moss and Gillespie noted their similarity to those of dioxane poisoning reported by Barber and de Navasquez. Subsequent studies have but served to emphasize the essentially identical pathologic effects in the kidneys and livers of human beings poisoned by Elixir of Sulfanilamide, and of animals given toxic

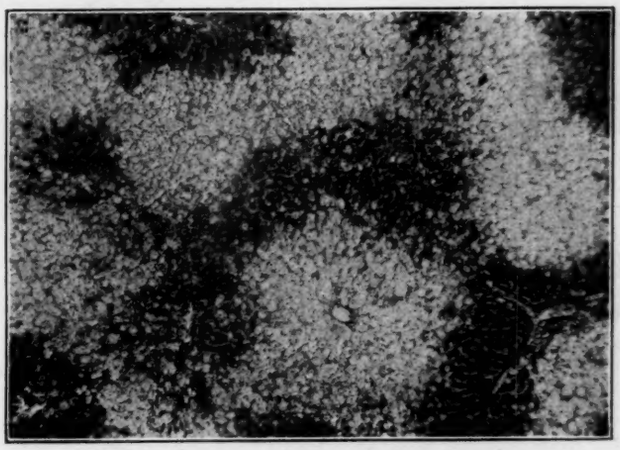


Fig. 10 (case 12).—Section of the 2,430 Gm. liver showing focal central hydropic degeneration of hepatic cells with absence of cellular disintegration. Note the shrunken pyknotic nuclei in the areas of hydropic degeneration. Reduced from a photomicrograph with a magnification of 60 diameters.

doses by mouth of either dioxane or diethylene glycol. There are apparently no known chemical substances other than these particular glycols which cause such a distinctive type of pathologic lesion in the liver and kidney.

The composite results of necropsy in these twelve cases may be summarized as follows: In several there was generalized edema (ascites, hydrothorax, hydropericardium and edema of the lungs) and, in some, recent hemorrhages into the gastrointestinal tract and lungs, evidences of increased capillary permeability,

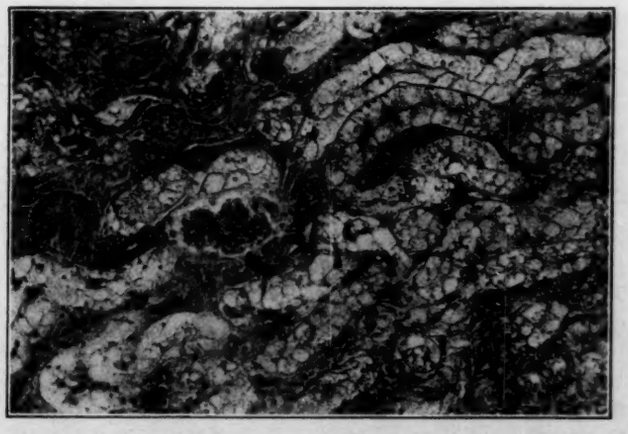


Fig. 11 (dog 6).—Section of the kidney of a dog given 0.8 Gm. per kilogram of body weight of Elixir of Sulfanilamide-Massengill over a period of four days. It died with symptoms of loss of appetite, vomiting, rigidity of the hind legs, weakness, dyspnea, coma, opisthotonos, extensor rigidity of front legs and deviation of the head to the right. Note the diffuse hydropic degeneration of the epithelium of the convoluted tubules and the obliteration of the lumens, just as in the human fatal cases. Reduced from a photomicrograph with a magnification of 225 diameters.

presumably from the acidosis and uremia. Bronchopneumonia occurred in some patients but not in all. The principal pathologic changes were in the kidney and liver. The former was enlarged in all twelve cases and in one (case 12) weighed 500 Gm. In eight of the

twelve symmetrical cortical necrosis with recent hemorrhage, particularly at the corticomedullary border, was the conspicuous feature (figs. 1 and 2). These cortical infarcts were absent in the kidneys of one adult and in three children between the ages of 2 and 6 years. The kidneys were described as flabby, pale and swollen, and their surfaces bulged after sectioning.

Fig. 12 (dog 7).—Section of kidney of a dog given 2.3 cc. of diethylene glycol by mouth per kilogram of body weight, three times a day over a period of seven days. The dog died with symptoms of weakness, loss of appetite, vomiting and tremors. Note the hydropic degeneration of tubular epithelium in the convoluted tubules. Reduced from a photomicrograph with a magnification of 225 diameters.

Microscopic examination revealed an unusual type of chemical nephrosis, the characteristic lesion being a severe vacuolation of the epithelium of the convoluted tubules, the so-called hydropic degeneration (figs. 3, 4 and 5). These cells appear "ballooned," as if the cytoplasm of each cell were a bag of water and there were no cytoplasmic material left to take the stain. The nuclei in such cells are shrunken and pyknotic and are absent in some. This profound swelling leads to complete obliteration of the lumens, and the anuria and uremia are most reasonably explained on the basis of mechanical stoppage of the flow of urine. Actual necrosis is not conspicuous in such cells, although some contain granular eosinophilic material in the cytoplasm, and there is some nuclear disintegration. The general picture suggests a "water-logging" of the cells rather than an effect of an extremely toxic protoplasmic poison. In some kidneys the epithelium of the convoluted tubules looks collapsed, as if the hydropic cells had ruptured and had liberated their contents. Here the lumens were open but seemed to be functionless. In other kidneys the hydropic degeneration was less conspicuous in some areas and here the convoluted tubules were lined with flattened cells in which at times were mitotic figures or giant nuclei, indicating attempts at regeneration. The glomeruli, in general, were but little affected except as they participated in the vascular changes associated with the cortical necrosis. In these areas of recent infarction the blood vessels, both small arteries and veins, contained hyaline thrombi, and the walls of many exhibited hyaline necrosis (figs. 6, 7 and 8). The infarcted area was infiltrated and surrounded by accumulations of red blood cells, and the tubules showed the characteristic changes of coagulation necrosis. Leukocytes were infiltrating these areas, although not more so, apparently, than is usual in an area of infarction. The collecting tubules usually contained hyaline casts, erythrocytes and accumulations of leukocytes. Fat stains showed practically no fatty degeneration in the areas of hydropic degeneration.

The mechanism of action of diethylene glycol as it passes through the kidney is still uncertain. In view of the fact that diethylene glycol is a hygroscopic agent, owing presumably to the two hydroxyl groups in its molecule, we suggested in our preliminary report that its presence within the epithelial cell might cause intracellular absorption and retention of water with consequent intracellular edema. Furthermore, because it is an ether, dihydroxy-diethyl ether, its solvent powers may cause injury to the cell membrane, followed by imbibition of water from the surrounding fluids. Evidence has been put forward [18] that in the glycol group "only those containing one or more ether linkages cause hydropic degeneration of parenchymatous cells." The adverse effects in the kidneys, therefore, are apparently due more to the mechanical closure of the lumens from the swelling of the cells than to actual necrosis in its most severe aspects, although such a profound involvement of parenchymatous cells causes death of cells, particularly if the effect is intense or prolonged.

The circulatory changes leading to infarction, hyaline necrosis of blood vessel walls and thrombosis may be explained as secondary phenomena due to blood stasis and tissue anoxia following swelling of the kidney, although a direct toxic action of diethylene glycol cannot be excluded. It is interesting that the vascular changes have occurred mainly in human beings and to but a slight degree in the experimental animals. The similarity to the so-called symmetrical cortical necrosis of the kidneys is striking. Scriver and Oertel,[19] in their discussion of this condition, have suggested that it is probably due to "vasoparalysis of terminal arterial segments with resulting blood stasis and segmentary thrombosis with proximal extensions" due to strong irritation of the vascular segments, an explanation in harmony with the experiments of Ricker and his students.[19] A similar effect may result from the action of diethylene glycol. De Navasquez [20] more recently has

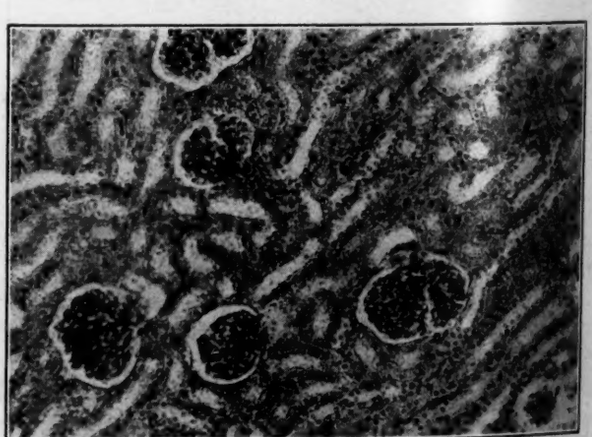


Fig. 13 (dog 3).—Section of the kidney of a dog given 0.2 Gm. per kilogram of body weight of sulfanilamide by mouth three times a day. The dog was killed eight days later. Note the essentially normal convoluted tubules and glomeruli with no evidences of hydropic degeneration or other degenerative change as revealed by hematoxylin and eosin stain. Reduced from a photomicrograph with a magnification of 225 diameters.

18. Kesten, H. D.; Mulinos, M. G., and Pomerantz, Leo: Pathologic Effects of Certain Glycols and Related Compounds, Arch. Path. **25**: 759-760 (May) 1938.

19. Scriver, W. de M., and Oertel, Horst: Necrotic Sequestration of the Kidneys in Pregnancy (Symmetrical Cortical Necrosis), J. Path. & Bact. **33**: 1071-1094 (Oct.) 1930.

20. de Navasquez, S.: Bilateral Cortical Necrosis of the Kidney in Pregnancy, J. Path. & Bact. **41**: 385 (Nov.) 1935.

concluded that the symmetrical cortical necrosis of the kidneys described by Barber [7] in human cases of dioxane poisoning was histologically identical with cortical necrosis of pregnancy. He thought also that in both conditions the necrosis of the walls of the intralobular arteries and their efferent glomerular branches led to ischemia and necrosis of the parenchyma.

stains, however, showed practically no fat in these cells, fatty degeneration occurring only in the hepatic cells at the margins. The nuclei were shrunken and pyknotic but not disintegrating, as a rule, though in some there was nuclear fragmentation, indicating a moderate degree of actual necrosis. Inflammatory infiltrations of leukocytes were minimal, if present at all (figs. 9 and 10).

TABLE 1.—*The Effect on Rabbits of the per Kilogram Equivalent of the Clinical Doses of the Elixir of Sulfanilamide-Massengill and the Corresponding Amounts of Diethylene Glycol*

Drug Given	Rabbit Number	Weight in Kilograms	Number of Days of Treatment	Total Number of Doses Given	Total Amount of Drug in Cc. Given per Kilogram of Body Weight	Day of Appearance of the Following Symptoms and Death							
						Apathy	Poor Appetite	Anuria	Refusal of Food	Prostration	Convulsions	Coma	Death
Elixir of Sulfanilamide-Massengill	1A	2.09	2	10	2.5	3	..	3	3	5	7	7	8
	2A	2.51	2	10	2.5	..	..	..	..	..	..	..	..
	3A	1.75	2	10	2.5	2	..	2	3	..	..	4	4
	7B	2.12	4	16	4.14	2	3	4	..	5	..	6	6
	1E	1.97	17	55	14.8	3	..	..	..	..	..	..	..
	3E	1.28	17	55	14.8	9	16	17	18	18	..	19	21
Diethylene glycol	1C	2.17	2	10	1.86	4	4	3	5	6	6	7	8
	7C	2.36	2	10	1.86	..	..	..	..	..	..	..	..
	6D	2.5	17	55	11.16	..	..	..	..	..	..	..	..
	3H	2.12	..	1	1.86	..	..	3	4	3	..	8	8
	4H	1.84	..	1	1.86	..	..	..	..	..	..	..	..
	1R	2.05	..	1	10.00	..	..	2	1	..	..	2	2
	4R	2.7	..	1	10.00	..	..	..	..	..	..	..	..

TABLE 2.—*Summary of Cases Reviewed*

Case	Age	Diagnosis	Amount Prescribed	Amount Taken	Comment	Autopsy by
1	24	Encephalitis.....	4 oz. Oct. 6, 1937; teaspoonful in water every 4 hours	Approximately 2 oz. from Oct. 7-11, 1937	Symptoms of poisoning began Oct. 11, 1937; sent to hospital Oct. 13, died Oct. 15	Dr. O. E. Hagebusch
2	3	Gonococcic urethritis, inguinal adenitis	1 oz. in 4 oz. mixture; teaspoonful in little water 4 times a day	Approximately 2 oz. of mixture	Symptoms of poisoning began 3 days after first dose; died Oct. 16, 1937	Dr. O. E. Hagebusch
3	6	Streptococcic sore throat	1½ oz. in 4 oz. mixture; teaspoonful in water	Approximately 2 oz. of mixture	Symptoms began Oct. 9, 1937, prescription stopped Oct. 11; died Oct. 18	Dr. O. E. Hagebusch
4	..	Epididymitis.....	4 oz. Oct. 9, 1937; teaspoonful in a little water every 4 hours	Approximately 3 oz.; broke first bottle and had refilled without consulting physician; took ½ oz. from second bottle at which time physician called	Symptoms Oct. 13, 1937; stopped taking medicine Oct. 14; died Oct. 21	Dr. O. E. Hagebusch
5	..	Cystitis; enlarged prostate	4 oz.; teaspoonful in half glass of water	Approximately 2 oz.	Stopped prescription Oct. 12, 1937; died Oct. 18	Dr. O. E. Hagebusch
6	64	Obscure kidney infection	3 oz.; teaspoonful in half glass of water	Approximately 2 oz.	Symptoms Oct. 15, 1937; Died Oct. 21	Dr. Ralph Monger
7	..	Chronic gonorrhea.....	5 oz. sulfanilamide tablets; took large dose of magnesium sulfate	Not ascertained	Admitted to hospital Oct. 8, 1937; died Oct. 10	Dr. Ralph Monger
8	30	Not stated.....	4 oz. Oct. 6, 1937	4 oz.	Died Oct. 13, 1937	Dr. K. M. Lynch
9	10	"Sore throat".....	4 oz. Sept. 24, 1937	Not ascertained	Died Oct. 12, 1937	Dr. K. M. Lynch
10	12	"Sore throat".....	2 oz. Sept. 24, 1937 (additional amount purchased without prescription)	4 oz.	Died Sept. 30, 1937	Dr. K. M. Lynch
11	62	Pyelitis.....	4 oz.; 2 teaspoonfuls every 4 hours for first 24 hours; then 1 teaspoonful every 4 hours, Oct. 9	2½ oz.; discontinued Oct. 16, 1937	Symptoms Oct. 15, 1937; died Oct. 20	Material from R. L. Thompson
12	29	Acute gonorrheal infection	6 oz.; 2 teaspoonfuls every 4 hours, Oct. 1, 1937	4½ oz.	Symptoms Oct. 4, 1937; stopped taking medicine Oct. 4; died Oct. 9	Dr. M. P. Kelsey

The livers were recorded as enlarged in all cases but one (case 6), in which it weighed only 900 Gm. The largest liver was found in case 12, in which it weighed 2,430 Gm. They were described as "tawny" or yellowish, although not bile stained, with pale, soft surfaces which bulged after sectioning. They presented the opposite picture of chronic passive congestion in that the centers of the lobules were light colored and the peripheries were darker. Microscopic examination revealed in all a central hydropic degeneration of the hepatic cells, with the cells "ballooned" and with the cytoplasm practically devoid of stainable material. Fat

The changes found in other organs were insignificant, other than congestion and hemorrhages of the stomach and intestine, which may have been a late effect of the uremia and terminal heart failure.

The similarity in dogs between the effects of diethylene glycol alone and of comparable amounts of Elixir of Sulfanilamide are shown in figures 11 and 12, where the extensive hydropic degeneration of epithelium of the proximal convoluted tubules is well seen. That the effect is not due to sulfanilamide alone is shown in figure 13, the reproduction of a photomicrograph from the kidney of a dog given twenty-one doses of sulfanil-

amide by mouth, 0.2 Gm. per kilogram three times a day. The kidney is essentially normal so far as hematoxylin and eosin staining is a criterion. As a matter of fact, frozen sections and fat stains showed a moderate fatty degeneration of epithelium in the collecting tubules, most marked near the corticomedullary border but minimal in the tubules most affected by diethylene glycol.

COMMENT

The similarity between the clinical course and the pathologic picture of the fatal human cases and that observed by us in the experimental animals affords conclusive proof that the chief toxic agent in Elixir of Sulfanilamide was the diethylene glycol. We showed this substance to have a cumulative effect. Evidently the time interval between doses and the concentrations in which the elixir was recommended for human use exceeded the capacity of the body to handle the drug without producing serious injury.

Experiments are now in progress to determine the manner of excretion and the levels at which different species of animals can handle diethylene glycol.

We are permitted to state that Dr. Herbert O. Calvery, chief pharmacologist of the Food and Drug Administration, Washington, D. C., and his staff are conducting experiments which are in general accord with our own observations.

The fact that increasing numbers of new chemicals are being introduced into therapeutics serves to direct attention anew to the necessity of adequate toxicologic studies on such compounds which are to be used in medical practice. It is only by precautions of this sort that future tragedies similar to the elixir episode will be avoided. The new food and drug act is intended to prevent, so far as possible, the introduction of new remedies which have not been satisfactorily tested on experimental animals. It is unfortunate that, in the past, too many drugs have been introduced for use in human beings without adequate preliminary studies of their possible injurious effects, and in some instances drugs have been indiscriminately marketed without any preliminary knowledge of their toxic potentialities.

A satisfactory program of preliminary trials for a new drug was outlined by Leake [21] in a discussion of drug policy presented before the Section on Pharmacology and Therapeutics of the American Medical Association at its annual session in 1929. It is interesting to note the clearness with which Leake anticipated the conditions responsible for the elixir episode as described in the government report.[22] In his paper, he states, "many drug firms make the mistake of believing that their chemists can furnish trustworthy pharmacologic opinion. Indeed, some eminent chemists, impatient with careful pharmacologic technic, have ventured to estimate for themselves the clinical possibilities of their own synthetics. . . . There is no short cut from chemical laboratory to clinic, except one that passes too close to the morgue."

It is important to recognize that, in the examination of a drug with a view to its use in therapeutics, the following conditions are essential:

1. If at all possible, the exact composition (qualitative and quantitative) should be known; or, if not obtainable, the detailed method of preparation of the product.

2. Acute toxicity studies on a sufficient number of laboratory animals of different species should be made; studies on one species alone may be very misleading.

3. Chronic toxicity experiments at varying dosage levels and with different species must be performed in order that any possible cumulative effect of the drug may be noted.

4. Careful and frequent observations of the animals are necessary, so that a composite picture of the clinical course is available. The data on many drugs are very deficient in this respect.

5. Careful pathologic examination of the tissues with appropriate stains is necessary.

6. Effects of the drug on animals with experimental lesions of various important excretory or detoxifying organs, especially of the kidneys and liver, should be studied.

7. The rate of absorption and elimination of the drug, its path and manner of excretion, and the concentration levels in the blood and tissues at varying times after administration must be determined.

8. The possible influence of the presence of certain foodstuffs or drugs should be noted. For example, magnesium sulfate should not be administered to a patient undergoing treatment with sulfanilamide.

9. Careful examinations for idiosyncrasies or untoward reactions should be made.

It is recognized that some will consider these safeguards to be too rigid and that they may simply be considered an ideal. It can correctly be charged, in fact, that some of the pharmacopeial drugs have not been studied along such lines. Admitting this, it is nevertheless regrettably true that many human lives have been sacrificed by the failure to meet the standards of these preliminary tests and that many more lives will be sacrificed if such standards are not put into effect. Any essential compromise with these requirements will inevitably exact a toll of deaths or injuries among the public. The life and safety of the individual should not be subordinated to the competitive system of drug exploitation.

The Elixir of Sulfanilamide catastrophe should once again serve as a warning to physicians who so readily prescribe unofficial drugs. There is no good reason why physicians should not have recourse to the simple expedient of prescribing only official or Council accepted preparations. By so doing they not only safeguard their patients but place their own influence solidly in favor of rationalized therapeutics. In addition, such a policy will tend to deemphasize the present enormous expenditures for advertising exploitation and tacitly direct drug manufacturers toward using their resources for the development of new and genuinely valuable agents in the treatment of disease. (Nonessential modifications of established drugs have no place in modern therapeutic practice.)

CONCLUSION

The intelligent, energetic and cooperative manner in which the representatives of the American Medical Association, of the Food and Drug Administration of the U. S. Department of Agriculture and of cooperating educational institutions worked brought this episode to a speedy solution. Had it not been for their splendid service the toll of human life would probably have amounted to several hundreds.

21. Leake, C. D.: The Pharmacologic Evaluation of New Drugs, J. A. M. A. **93**: 1632 (Nov. 23) 1929.

22. Report of the Secretary of Agriculture on Deaths Due to Elixir of Sulfanilamide-Massengill: How the "Elixir" Was Produced, Document 124, 1937, p. 203.

Special Article

VITAMIN B_1

METHODS OF ASSAY AND FOOD SOURCES

HAZEL E. MUNSELL, PH.D.

WASHINGTON, D. C.

This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—ED.

The importance of vitamin B_1 in physiology and pathology has emphasized markedly the need of devising accurate methods for the quantitative determination of this substance in foods. Until recently the chemical identity of vitamin B_1 was unknown, rendering it impossible to develop chemical methods of analysis, and accordingly recourse was had to biologic methods of assay using rats and pigeons as test animals. Much information regarding the vitamin B_1 content of foods has been gained in this way, especially by the method in which the growth of rats was used as the measure of potency. This paper presents the technical aspects of various methods of bio-assay for vitamin B_1 from the point of view of quantitative interpretation of the results obtained and discusses briefly the chemical methods that are being developed. It concludes with an evaluation of foods as sources of the vitamin.

BIOLOGIC METHODS WITH PIGEONS

The first methods devised for the assay of vitamin B_1 were based on the prevention or cure of polyneuritis in pigeons.[1] There was also developed the weight maintenance method,[2] which involved the determination of the minimum amount of a substance required to maintain the weight of a standard bird on a polished rice diet. Because of many experimental difficulties, these methods are now used by only a limited number of investigators. The preventive method lacked specificity and the results were far too variable to admit of satisfactory quantitative analysis. The weight maintenance method raised the question of whether the antineuritic factor (vitamin B_1) and the growth factor were identical.[3] Although the curative method has been used more extensively than the others, it has not proved to be more than fairly satisfactory owing to several major difficulties, such as irregularity of appearance of polyneuritis, the development of multiple deficiencies because of the inadequacy of the polished rice diet, development of nonspecific symptoms due to inanition, temporary and spontaneous remission of symptoms, failure of cures and variability in the time of response in different birds. In this connection it is interesting to note that the prevention of polyneuritis in young chicks was recently suggested as a means of assaying for vitamin B_1.[4]

The methods referred to are described in the literature in more or less final form and it seems unnecessary to present them in detail here. However, certain results obtained with the pigeon curative technic, more especially those concerned with the derivation of quantitative values, are or may be paralleled in the rat curative method which is now under investigation by the Committee of Revision of the U. S. Pharmacopeia. It seems advisable, therefore, to review briefly the results obtained with the pigeon curative technic on the basis of their experience value.

In the procedure with the pigeon curative technic there seem to be several items directly influencing the results obtained. The magnitude of the response of the birds to test doses of vitamin B_1, for instance, is conditioned not only by the quantity of vitamin B_1 administered but also by such factors as the nature of the basal diet used, the duration of the initial depletion period and the duration of vitamin B_1 administration.[5] The method of administration of crystalline vitamin B_1 also affects the results in that the response to doses administered by injection is greater than the response to doses of the same size given orally.[6]

Several methods have been used or suggested for expressing the results of the assays quantitatively. In the very early tests, attempts were made to assess values by determining the minimum quantity (minimum curative dose) of the substance required to cure induced symptoms of polyneuritis. This procedure did not prove to be satisfactory because in practice it was not possible to define "minimum curative dose."[7] It soon became apparent also that the responses of different birds to like amounts of vitamin B_1 bearing material vary widely and that direct comparisons can be made only from successive tests with the same bird.

Further studies were then made to determine the relation between the size of the curative dose of vitamin B_1 administered and the duration of cure. Evidence was presented[8] to show that there is a direct quantitative relation between the dose and the duration of cure, i. e., the number of days of protection after cure before the onset of the next attack. In the application of this finding to the comparison of results with different substances, an attempt was made to reduce them to a comparable basis by expressing the relative potencies in terms of day doses per gram of material.[9] Values obtained from results with different dose levels of a given substance showed wide differences, however, and it was later concluded that this procedure is not a valid one.[6] The reason for this becomes clear when it is

1. Emmett, A. D., and Peacock, G. E.: Adequacy of Pigeons and Rats for Vitamin B Studies, J. Biol. Chem. **63:** xxiii (Feb.) 1925. Kinnersly, O'Brien and Peters.[6] Coward, Burn, Ling and Morgan.[7]

2. Seidell, Atherton: A Physiological Test for the Activity of Vitamin Preparations, Pub. Health Rep. **37:** 1519 (June 23) 1922. Plimmer, R. H. A.; Raymond, W. H., and Lowndes, John: Comparative Vitamin B_1 Values of Foodstuffs: Fruits and Vegetables, Biochem. J. **25:** 1788, 1931. Block, R. J.; Cowgill, G. R., and Klotz, B. H.: The Antineuritic Vitamin: I. The Method of Assay, Concentration of the Vitamin with Silver Under Various Conditions, and Its Solubility in Certain Organic Solvents, J. Biol. Chem. **94:** 765 (Jan.) 1932.

3. Smith, M. I.: A New Method of Evaluating the Potency of Antineuritic Concentrates, Pub. Health Rep. **45:** 116 (Jan. 17) 1930.

4. Arnold, Aaron, and Elvehjem, C. A.: Studies on the Vitamin B_1 Requirements of Growing Chicks, J. Nutrition **15:** 403 (April) 1937.

5. Carter, C. W., and O'Brien, J. R.: Maintenance Nutrition in the Pigeon: The Effect of Vitamin B_1, Biochem. J. **31:** 2264 (Dec.) 1937. Waterman, R. E., and Ammerman, Marion: Studies of Crystalline Vitamin B: VI. The Effect of Graduated Doses on Pigeons, J. Nutrition **10:** 161 (Aug.) 1935.

6. Kinnersley, H. W.; O'Brien, J. R., and Peters, R. A.: Crystalline Vitamin B_1, Biochem. J. **29:** 701 (March) 1935.

7. Coward, K. H.; Burn, J. H.; Ling, H. W., and Morgan, B. G. E.: The Determination of the Antineuritic Vitamin, Biochem. J. **27:** 1719 (No. 5) 1933.

8. Kinnersley, H. W.; Peters, R. A., and Reader, Vera: Antineuritic Yeast Concentrates: III. The Curative Pigeon Test: A Critique, Biochem. J. **22:** 276 (No. 1) 1928.

9. Kinnersley, H. W.; Peters, R. A., and Reader, Vera: A Quantitative Comparison of the Curative Activity of Torulin (Vitamin B_1) upon the Adult Pigeon and the Adult White Rat, Biochem. J. **24:** 1820 (No. 6) 1930.

recognized that the relation of the duration of cure to weight of material given is not represented by a straight line.[7] It has been shown, however, that it is possible to derive a curve of reference representing the relation of duration of cure to quantity of vitamin B_1 ingested that is valid for use in interpreting results obtained by the curative method.[7]

Other estimates from data obtained with the pigeon curative method have been made on the basis of percentage of birds cured [7] and the degree of accuracy in these values was shown to be as great as in those computed on the basis of duration of cure.

The chief points to consider in judging the worth of a biologic method are its specificity, its precision and its sensitivity. In the curative method, precision is contingent on the determination of the length of the curative period, which in turn depends on the determination of the time of onset of the symptoms of polyneuritis. Even if the symptoms indicating the onset of polyneuritis could be exactly described, frequent periodic observation during the entire twenty-four hours of a recorded day would be necessary to ascertain the exact time of onset. In most laboratories such complete observations are not possible and the recorded time of onset of symptoms at the beginning and at the end of the curative period may be considerably in error. Thus the value given as the duration of the cure may involve an error in recorded time, as well as errors arising from the use of birds given the curative dose at different stages of development of polyneuritis.

The sensitivity of the test is also not so great as might be hoped for. A tenfold increase in vitamin B_1 intake apparently extends the curative period from the minimum of two or three days to only six or seven days. It seems justifiable to say, therefore, that the method is seriously lacking both in preciseness and in sensitivity.

Catatorulin Effect.—During the course of studies in which pigeons were used to determine the potency of vitamin B_1 concentrates, it was observed that the oxygen uptake of brain tissue from avitaminous pigeons increased on the addition of concentrates of vitamin B_1 in lactate solution.[10] This was interpreted to be in the nature of a catalytic effect and the active factor was designated catatorulin although there was strong evidence that it was identical with vitamin B_1. A technic was devised whereby the effect of the vitamin B_1 containing substance on the oxygen uptake of excised pigeon's brain was used as an index of the quantity of vitamin B_1 present.[11] The curve relating the dose of vitamin B_1 (micrograms to 3 cc. of solution) to oxygen uptake (milligrams per gram hourly), although not a straight line, was a smooth curve similar to the one relating vitamin B_1 intake to growth in rats. The catatorulin test has been suggested as a most promising one for comparing the potencies of vitamin B_1 containing substances, although further study is required to perfect the method.[6]

BIOLOGIC METHODS WITH RATS

The Growth Test.—The use of growth in the rat as a means of detecting the presence of vitamin B_1 in substances was suggested as early as 1918. The method developed by Sherman and Spohn [12] and more especially the basal diet worked out by them was generally used up to the time when it was shown that for normal growth the rat requires in addition to vitamin B_1 a heat stable fraction remaining in autoclaved yeast. The Sherman and Spohn basal diet was then modified by Chase [13] to include sufficient autoclaved yeast so that vitamin B_1 was the first if not the only growth limiting factor.

The use of a preliminary depletion period was also suggested at this time as a precautionary measure even though it is generally agreed that vitamin B_1 is not stored in the body to any great extent and that animals given a vitamin B_1 free diet show only slight residual growth.

The procedure of the rat growth technic,[14] like that of any other method, is carried out more or less according to the tenets of the investigator who is using it. For the purpose of this discussion, however, it does not seem necessary to consider in detail the various conclusions and recommendations that have been made except so far as they have a direct bearing on the uniformity and reliability of the results obtained.

Essentially, the procedure consists in the keeping of healthy young rats of known lineage and within a given age and weight range on a diet devoid of vitamin B_1 but adequate in all other factors needed for growth. They are maintained on this diet without supplement either for a specified length of time considered sufficient for depletion or until there are evidences that their stores of vitamin B_1 have been depleted. The animals are then given daily (or six times a week) weighed quantities of the material under investigation during a test period of specified length. The gain in weight during this period is used as a measure of the quantity of vitamin B_1 present.

The reliability of the results from the rat growth method depends in large part on the selection and grouping of the experimental animals. The quantity of the standard material fed should be that which gives a growth response at or near the critical level, this being the gain in weight from which comparisons are to be made. In the Sherman-Chase method, for instance, the point corresponding to an average gain of 3 Gm. a week is used. This point is located in the steepest part of the curve relating gain in weight to dose of vitamin B_1 but far enough up on the curve so that all the experimental animals may be expected to survive. It is often the practice to administer the test material at three or more dose levels and the Standard of Reference material at one or more dose levels. The quantities of test material are so selected that one induces a growth response at or near the critical level, one above this and one below.

The animals to be given the several doses must be as nearly alike as possible. On identical quantities of vitamin B_1 the growth response of males is usually

10. Passmore, Reginald; Peters, R. A., and Sinclair, H. M.: On Catatorulin: A New Method of Comparing the Oxidative Factor in Vitamin B_1 Concentrates, Biochem. J. **27:** 842, 1933.

11. Peters, R. A.; Rydin, Hakan, and Thompson, R. H. S.: Brain Respiration, a Chain of Reactions, as Revealed by Experiments upon the Catatorulin Effect, Biochem. J. **29:** 53 (No. 1) 1935. Passmore, Peters and Sinclair.[10]

12. Sherman, H. C., and Spohn, Adelaide: A Critical Investigation and an Application of the Rat Growth Method for the Study of Vitamin B, J. Am. Chem. Soc. **45:** 2719 (Nov.) 1923.

13. Chase, E. F., and Sherman, H. C.: A Quantitative Study of the Determination of the Antineuritic Vitamin B, J. Am. Chem. Soc. **53:** 3506 (Sept.) 1931.

14. British Pharmacopeia, Biological Assay of Antineuritic Vitamin (Vitamin B_1), 1932, p. 91. Chase and Sherman.[13] Coward, K. H.: The Biological Standardization of the Vitamins, London, Baillière, Tindall and Cox, 1938.

greater than that of females.[15] Animals of different strain, or even litters of the same strain, may show differences in growth response for given quantities of vitamin B_1.[16] For these reasons it is also recommended that the series of graded test doses and the dose of the standard be allotted to littermate animals of the same sex of about the same weight. Additional litters of animals are then used until the number of individuals on each dose level is sufficient to give an average result having an acceptable degree of reliability.

In the original Sherman and Spohn technic a test period of eight weeks was used. It was felt later, however, that results from a shorter period might more truly represent an uncomplicated vitamin B_1 effect, free from influence of other unknown growth essentials that might not have been supplied in the basal diet. Accordingly, a four weeks period was suggested.[17] Results from a test period of two weeks have been reported to be very nearly as good as those from one of three weeks' duration.[18] With a low rate of gain, results have been obtained on the basis of a ten day period,[19] although a somewhat longer period than this would seem to be generally more satisfactory.

At the completion of the test the gains in weight for the individual animals in each group are determined and the average gains in weight for the different groups are calculated. If the test material contained vitamin B_1 the gains in weight will be graded to the dose. With crystalline vitamin B_1, for instance, growth has been shown to increase with doses as high as 160 micrograms per rat daily.[20]

From the results obtained a curve (curve of response or dose-effect curve) is drawn, relating gain in weight to quantity of material given. The smoothness of this curve will serve as an indication of the reliability of the test. The quantity of test material estimated to give the same effect, i. e. to have the same potency as the quantity of standard fed, is then derived from the curve of response, which is drawn to a suitable scale so that the degree of precision implied by the value derived is in accord with the values used in constructing the curve.

The degree of accuracy of vitamin B_1 estimated by the rat growth method has been studied statistically and is reported to be high for a method of this type.[18] The sensitivity also seems to be high, since it is possible to differentiate doses of crystalline vitamin B_1 differing in potency by only one microgram, although a dose of three micrograms must be administered before an appreciable growth response is obtained.[21]

Refection and Coprophagy.—One of the more serious difficulties involved in the vitamin B_1 assay is that of eliminating the extraneous source of vitamin B_1 to which the rat may have access as a result of "refection."[22] There is ample evidence for believing that vitamin B_1 may be formed in the cecum probably as the result of bacterial action on the food residues there.[23] Refection appears to be dependent on the starch component of the diet. Raw potato starch, for instance, has a high refective power, while rice, wheat and rye starches are reported to have little or none.[24] Cooking the starch seems to destroy its refective property.[25] The vitamin B_1 due to refection is not absorbed from the lower intestinal tract, but the rat may obtain benefit of it by the simple expedient of consuming his feces. The use of cages with large mesh screen bottoms tends to lessen this tendency but does not necessarily eliminate it altogether. One consoling feature with regard to refection is that it does not occur in all cases and a watchful observer can generally identify refected animals by the bulky character of the feces and a growth response not in accord with the known intake of vitamin B_1.

The Curative Technic.—Polyneuritis in rats was reported as early as 1917 and in the following year a method for vitamin B_1 determination was described in which rats were kept on the vitamin B_1 free diet until they showed declining weight or symptoms of paralysis or both. Hofmeister[26] in 1922 was the first, however, to report the consistent appearance of polyneuritis in large numbers of rats. Several years later a comparison of results by the pigeon test and the rat curative test led to the conclusion that the same factor was measured with rats as with pigeons.[9] About the same time Sandels,[27] using a basal diet containing adequate amounts of the heat stable components, reported that polyneuritis occurred in rats only when small quantities of vitamin B_1 were present in the basal diet. This point has since been corroborated by other investigators.[28]

The first plausible plan for vitamin B_1 determination based on the curative technic with rats was that described by Smith.[29] Rats from 50 to 70 Gm. in weight and from 30 to 40 days of age developed symptoms of polyneuritis in from fifty to eighty days. Vitamin B_1 administered orally or by injection produced improvement in from three to five hours and a definitely curative effect in from eighteen to twenty-four hours. When the curative effect of a given dose had worn off the symptoms of polyneuritis recurred and were again alleviated

15. Sherman, H. C., and MacArthur, E. H.: A Quantitative Study of the Determination of Vitamin B, J. Biol. Chem. **74:** 107 (July) 1927. Coward, Burn, Ling and Morgan.[7] Waterman and Ammerman.[20]

16. Light, R. F., and Cracas, L. J.: Vitamin B_1 Requirements of Different Strains of White Rats, Science **87:** 90 (Jan. 28) 1938.

17. Sherman, H. C., and Smith, S. L.: The Vitamins, New York, Chemical Catalog Company, 1931, p. 103.

18. Coward, K. H.: The Influence of the Length of the Test Period on the Accuracy Obtainable in a Vitamin B_1 Test, Biochem. J. **30:** 2012 (Nov.) 1936.

19. Schlutz, F. W., and Knott, E. M.: The Use of a Ten-Day Period for the Assay of Vitamin B by Rat Growth Technic, J. Nutrition **12:** 583 (Dec.) 1936.

20. Waterman, R. E., and Ammerman, Marion: Studies of Crystalline Vitamin B: V. The Effect of Graduated Doses on Growing Rats, J. Nutrition **10:** 35 (July 10) 1935.

21. Unpublished data of Bureau of Home Economics, U. S. Department of Agriculture.

22. Steenbock, Harry; Sell, M. T., and Nelson, E. M.: Vitamin B: I. A Modified Technic in the Use of the Rat for Determination of Vitamin B, J. Biol. Chem. **55:** 399 (March) 1923. Dutcher, R. A., and Francis, Emma: Vitamin Studies: X. Feeding Technic in Vitamin Studies, Proc. Soc. Exper. Biol. & Med. **21:** 189 (Jan.) 1924. Fridericia, L. S.; Freudenthal, P.; Gudjonnsson, S.; Johansen, G., and Schoubye, N.: Refection, A Transmissible Change in the Intestinal Content, Enabling Rats to Grow and Thrive Without Vitamin B in the Food, J. Hyg. **27:** 70 (Nov.) 1927.

23. Guerrant, N. B.; Dutcher, R. A., and Tomey, L. F.: The Effect of the Type of Carbohydrate on the Synthesis of the B Vitamins in the Digestive Tract of the Rat, J. Biol. Chem. **110:** 233 (June) 1935. Griffith, W. H.: Studies on Growth: III. B and G Avitaminosis in Cecectomized Rats, J. Nutrition **10:** 667 (Dec.) 1935.

24. Kon, S. K.: Potato Starch and Refection, J. Hyg. **31:** 543 (Oct.) 1931. Bliss, Sidney, with the technical assistance of Green, Fred: Refection in the Rat: With an Appendix on Methods of Preparing Basic Materials for Deficient Diets, J. Nutrition **11:** 1 (Jan.) 1936.

25. Roscoe, M. H.: Spontaneous Cures in Rats Reared upon a Diet Devoid of Vitamin B and Antineuritic Vitamin, J. Hyg. **27:** 103 (Nov.) 1927.

26. Hofmeister, Franz: Studien über qualitative Unterernährung: II. Mitteilung der experimentelle Nachweis des Antineuritins, Biochem. Ztschr. **129:** 477, 1922.

27. Sandels, M. R.: Experimental Nutritional Polyneuritis in the Rat, J. Nutrition **2:** 409 (March) 1930.

28. Sebrell, W. H., and Elvove, E.: Observations on the Assay of the Antineuritic Vitamin: Some of the Factors Involved in the Use of the Rat Method, Pub. Health Rep. **46:** 917 (April 17) 1931. Waterman and Ammerman.[30]

29. Smith, M. I.: A New Method of Evaluating the Potency of Antineuritic Concentrates, Pub. Health Rep. **45:** 116 (Jan. 17) 1930.

by a dose of the vitamin. It was suggested that the same animal might be used many times with little variation in its response to doses of equal potency. Although Smith found the curative effect proportional to the dose, the relationship was not considered quantitative and he made his comparisons, therefore, on the basis of the minimum curative dose. A cure lasting three days was considered the shortest remission period a minimum effective dose would bring about. The method was checked with a large number of substances and was considered to be entirely specific.

One particular advantage claimed for the foregoing method is the possibility of making comparative tests with the same animal, thus eliminating some of the errors due to differences in behavior of different test animals, a defect inherent in the rat-growth method. Several investigators working with the curative method have, however, reported considerable variation in the occurrence of polyneuritis and it is suggested that complete familiarity with the symptoms is essential before assay work is undertaken.[30] In this connection, criteria for judging the presence of polyneuritis have been described in detail and attention has been called to the fact that treatment of subsequent onsets may not always produce exactly the same result. The effect of such variation is reduced by the use of a sufficiently large number of animals.

To obtain greater uniformity in the occurrence of polyneuritis, the administration of known quantities of vitamin B_1 to each test animal has been recommended. Ammerman and Waterman,[31] for instance, suggest the daily injection of 0.5 microgram of crystalline vitamin B_1. Dann [32] uses a diet containing 400 Gm. of brewers' yeast per hundred pounds, which she claims gives a higher incidence of polyneuritis than the diets used by Ammerman and Waterman or Smith. Recent work [33] seems to indicate that the fat content of the diet may be an important factor in vitamin B_1 tests in relation to the production of polyneuritis in rats. A low incidence of polyneuritis was found among rats on a high fat diet, which is in accord with other observations on the fat-sparing action of vitamin B_1.

As already stated, studies for the purpose of selecting a suitable method for the assay of vitamin B_1 are at present being carried out under the direction of the Committee of Revision of the Pharmacopeia of the United States of America. Only the rat curative technic is being considered because a previous survey had indicated this to be the preferred method of the four procedures to which consideration had been given. Of the several modifications of the rat curative technic under investigation it seems necessary, however, to consider only the one in use at present in the Vitamin Division of the Food and Drug Administration of the United States Department of Agriculture.[34] This procedure is based on the one used by Smith, differing from it primarily in the use of a more adequate diet consisting of sucrose 61.25 per cent, casein 18.0 per cent, salt mixture I 4.0 per cent, autoclaved yeast 4.0 per cent, autoclaved peanuts 10.0 per cent, purified liver extract 0.75 per cent, and cod liver oil 2.0 per cent.

Sources of all known components of the vitamin B complex, including vitamin B_4 and factor W of Elvehjem, are presumably present in this diet. Special purification of the casein and the use of sucrose in place of starch are also new features. Although a known source of the minimal quantity of vitamin B_1 considered to be essential for the production of polyneuritis is not included in this diet, 100 per cent occurrence of polyneuritis in rats weighing from 40 to 70 Gm. is claimed for it. Furthermore it has been demonstrated that, with this diet, polyneuritis can be produced and cured repeatedly in the same animal, the production of ten or more such periods in a single animal being quite usual.

The details of the test may be summarized briefly. The basal diet is given to litters of rats from 12 to 13 days of age, which are kept with their mothers in cages having raised screen bottoms. The young are weaned when they weigh between 40 and 50 Gm. and are weighed weekly until the twenty-fifth day. At the end of this period they are put in individual cages, weighed daily and observed for symptoms of polyneuritis, which are classified as slight, acute or severe. Only animals in the acute stage are used in an assay.

When an animal is judged ready for the test, 2 international units of vitamin B_1 are administered and the weight and condition of the animal are again noted daily. The time elapsing between the administration of the curative dose and the recurrence of polyneuritic symptoms is designated the curative period. At the second occurrence of acute polyneuritis, a dose of the test material is given and the length of the curative period is recorded as before. In Kline's experience 2 international units of vitamin B_1 gives a curative period of from seven to eleven days with animals ranging in weight from 40 to 70 Gm. at the time the curative dose is administered.

Results obtained in the assay of crystalline vitamin B_1 by this method show that the duration of cure following administration of vitamin B_1 increases with increasing dosage. For a considerable range the relationship is linear, although at higher levels the curve flattens off as do other dose-effect curves showing the behavior of animals to graded doses of a given vitamin. In successive periods with the same animal the length of the curative period for a given dose of crystalline vitamin B_1 was found to be uniformly reproducible to a remarkable degree. Thus it was considered possible to use the length of the curative period as an accurate measure of the vitamin B_1 administered in a test dose. Errors due to variation of animals are eliminated by using the results of successive trials with the same animal to compare the potency of the test material with that of the standard.

In an assay performed in this way a given quantity of the test substance is considered to contain at least 2 international units of vitamin B_1 if it promotes in the experimental animals a total curative period (the sum of the days of the curative period of each of the animals) equal to or greater than the total curative period following the feeding of an amount of the international standard equivalent to 2 units. "If it is desired to determine the exact potency of an unknown [test material], it is preferable to feed it to a few animals at

30. Heyroth, F. F.: The Evaluation of Vitamin B_1 Concentrates by the Rat Cure Method, Bull. Basic Science Research **4**: 1, 1932.

31. Ammerman, Marion, and Waterman, R. E.: Studies of Crystalline Vitamin B: IV. Injection Method of Assay, J. Nutrition **10**: 25 (July) 1935.

32. Dann, Flemintine P.: Vitamin B Assay Using Rat Curative Method with Modified Diets and Oral Administration of Addenda, J. Nutrition **12**: 461 (Nov.) 1936.

33. McHenry, E. W.: An Effect of Choline on the Vitamin B_1 Sparing Action of Fats, Biochem. J. **31**: 1616 (Sept.) 1937. Salmon, W. D., and Goodman, J. G.: Alleviation of Vitamin B Deficiency in the Rat by Certain Natural Fats and Synthetic Esters, J. Nutrition **13**: 477 (May) 1937.

34. Kline, O. L.; Tolle, C. D., and Nelson, E. M.: Vitamin B_1 Assay by a Rat-Curative Procedure, J. A. Off. Agric. Chem. **21**: 305 (May) 1938.

various levels to determine the approximate quantity which contains two international units of vitamin B_1. The assay should then include successive feedings of the standard and unknown [test material] on at least eight animals." It is the opinion of the sponsor of this method that it is the most accurate procedure for vitamin B_1 determination that has been proposed.

Several measures other than duration of cure have been used for the quantitative expression of results from the rat curative technic. One of the first was weight recovery time,[30] i. e. the time required for the rat to return to the weight it showed when the injection of vitamin B_1 was made. Another measure used is the number of day doses per gram of material.[9] This value is derived in the same way as in the method with pigeons and is therefore subject to the same limitations.[35] Reference has already been made to the minimum curative dose used in the method described by Smith.[29] Although this measure is more logical than the determination of day doses it involves the same difficulties associated with the determination of the minimum curative dose for pigeons.

The Bradycardia Method.—In 1929 a condition of heart block and bradycardia preceding appearance of symptoms of polyneuritis or head retraction was reported in pigeons fed polished rice. The following year a condition of bradycardia in rats was described[36] which did not seem to be due to lowered food intake but rather to the effects of lack of vitamin B complex, since the condition did not occur in controls on a restricted food intake. It was cured by administration of vitamin B_1. A special device for taking electrocardiograph records had been designed and the average normal heart rate for the rat was determined as from 500 to 530 per minute. Rats maintained on a vitamin B_1 free diet for about two weeks showed a gradual slowing of the heart rate, which finally reached a low level of 250-300 beats per minute. On the administration of vitamin B_1[37] the rate returned to normal and remained so for several days, when it began to fall again. The degree of recovery was "related" to the quantity of vitamin B_1 available.

Following this a method for the quantitative determination of vitamin B_1 based on the remission of bradycardia in rats was suggested.[38] In this method young rats weighing about 40 Gm. are given a vitamin B free diet and after about three weeks, or when loss of weight begins, electrocardiograms are taken. As soon as a heart rate of 350 beats per minute is recorded, the test sample is given and "dosing" is repeated until there is an increase in the rate. Thereafter, readings are taken every twenty-four hours until the heart rate has fallen again to the level recorded at the beginning. Both the increase in rate and the duration of the increased rate were found to be proportional to the dose administered. Cures of four days' duration are considered most satisfactory. Tests are made at several levels with from four to six animals at each level and a dose-effect curve is plotted. Comparisons are made to determine the quantities of the international standard that give the same effect. An activated clay product, yeast, marmite and wheat germ, were assayed by the procedure described and also by the rat curative method, the rat growth method and the pigeon technic. The results by all four procedures agreed.[38]

The advantages claimed for the bradycardia method are a short preparatory period, ease and rapidity in obtaining results, and economy in test animals since one animal may be used for several tests. The sensitivity is considered to be only slightly less than that of the growth method. The investigators admit that the chief drawback to the general use of this method is the expense of the electrocardiograph. It has been used by Baker and Wright[39] for the assay of about a hundred different foods. With 20 and 30 mg. of the International Standard of Reference, the method was considered accurate to within ± 20 per cent. Cures giving responses of about 450 beats per minute tended to be prolonged or irregular. The responses to the first test doses tended to be abnormal and these results, therefore, were discarded. The values reported by these investigators are in general somewhat higher than values given for similar products by other investigators.

The original proponents of this method have made a thorough study of it in a determination of the potency of crystalline vitamin B_1 preparations and have also used it extensively and apparently successfully in studies of the urinary excretion of vitamin B_1.[40] In the hands of others, however, it has not fared so well. Robertson and Doyle,[41] who attempted to use it in the assay of a crystalline vitamin B_1 preparation, observed considerable fluctuation in individual animals. A single tracing, for instance, showed a rate in one part that was forty beats per minute higher than the rate in another part, and two tracings from one rat showed differences of 100 beats per minute. Another rat on a curative dose of 6 micrograms showed rates varying from 326 to 480. R. S. Harris,[42] working with a carniotachometer designed for the purpose, has found discrepancies of even greater magnitude in normal and in vitamin B_1 deficient rats.

QUANTITATIVE INTERPRETATION OF RESULTS BY THE BIOLOGIC METHODS

The variety of assay procedures described naturally makes one query concerning the quantitative interpretation of results. Those obtained in the early studies in which pigeons were used were interpreted either directly in terms of the curative dose, as already explained, or in relation to the potency of some other substance such as yeast assigned an arbitrary value, for example 1, 10 or 100. These data are difficult, if not impossible, to reconcile with values obtained by other methods and at most have little more than qualitative significance. It is probably safe to say that many of the data on the occurrence of vitamin B_1 obtained by the pigeon technic prior to the time of adoption of the international stand-

35. Heyroth, F. F.: The Use of Various Rat Assay Methods in Comparing Crystalline Vitamin B_1 Preparations, Biochem. J. **30:** 645 (April) 1936.

36. Drury, A. N.; Harris, L. J., and Maudsley, Cecil: Vitamin B Deficiency in the Rat: Bradycardia as a Distinctive Feature, Biochem. J. **24:** 1632 (No. 6) 1930.

37. An autolyzed yeast preparation (Marmite) was used.

38. Birch, T. W., and Harris, L. J.: Bradycardia in the Vitamin B_1 Deficient Rat and Its Use in Vitamin B_1 Determinations, Biochem. J. **28:** 602 (No. 2) 1934.

39. Baker, A. Z., and Wright, M. D.: The Vitamin B_1 Content of Foods, Biochem. J. **29:** 1802 (July) 1935.

40. Harris, L. J., and Leong, P. C.: Vitamins in Human Nutrition: The Excretion of Vitamin B_1 in Human Urine and Its Dependence on the Dietary Intake, Lancet **1:** 886 (April 18) 1936. Leong, P. C., and Harris, L. J.: Antineuritic Potency of Synthetic and Natural Crystalline Vitamin B_1 as Determined by the "Bradycardia" Method with a Statistical Study of the Degree of Accuracy of the "Bradycardia" Method, Biochem. J. **31:** 672 (April) 1937.

41. Robertson, E. C., and Doyle, M. E.: Difficulties in the Use of Bradycardia Method of Assaying Vitamin B_1, Proc. Soc. Exper. Biol. & Med. **37:** 139 (Oct.) 1937.

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ards have not been quantitatively evaluated. This may in part account for the dearth of tabulated vitamin B_1 values.

Two units other than the international unit have been defined for the interpretation of data by the rat growth method. The first was the maintenance unit, which was defined [43] as that amount of vitamin B_1 which, when fed as a daily allowance, results in net maintenance of a standard rat over an eight weeks period under the conditions described. Although this unit was never used extensively and there are few data reported in terms of it, Cowgill has referred to it in his discussion of equivalents and for this reason it seems advisable to mention it here.

The large majority of values for the vitamin B_1 content of foods as well as for other substances has been expressed in terms of the growth unit. This is defined [44] as that amount of vitamin B_1 which, when fed daily under experimental conditions as described, induces in a standard test animal an average gain of 3 Gm. a week during the test period. Values expressed in this unit have been derived from results obtained with the Sherman-Spohn diet as well as the Sherman-Chase basal diet. The Sherman-Spohn diet did not contain a supply of vitamin G sufficient for growth, and values obtained with this diet therefore may or may not indicate the full vitamin B_1 value of the substance tested, depending on whether the basal diet and the test substance supplied sufficient vitamin G for growth. Roscoe [45] used a somewhat higher rate of gain, from 10 to 12 Gm. a week, for the growth unit.

The introduction of the international standards has given a more precise method of expressing vitamin values than was possible before these standards became available. There is evidence, however, that estimates made in terms of international units are not always as precise as they might have been. The derivation of values by the use of standards of reference by any method of analysis involves the determination of quantities of standard and of test material that give the same effect. The accuracy of the assay depends on the closeness of this determination. Many investigators use the method of trial tests to determine the quantity of test material equivalent to a given quantity of standard. With the wide variations inherent in results obtained by biologic methods a close match is obtained only if great care is taken in carrying out the assay; and, even when such results seem to have been obtained, the reliability is even more difficult to check. A perusal of published data indicates that in this procedure more attention should be given to the adoption of criteria for determining the limits within which the two effects may be considered to be identical. Other investigators may use a dose effect curve, as described under the growth method with rats, from which the quantity of test material equivalent to the quantity of standard used may be estimated if the results of the assay do not give it directly. Such curves may involve large errors of estimate, however, unless consideration is given to factors giving rise to variation in results with different test subjects.

The recently completed assay of the crystalline vitamin B_1 hydrochloride proposed for international standard to replace the adsorbate now in use indicates that vitamin B_1 values for substances assayed against the international standard adsorbate vary according to the method of assay used. Values obtained by the curative technics, for instance, were considerably higher than values by the prophylactic or growth method. It is suggested that in sick animals such as those used in the curative method there is incomplete elution of vitamin B_1 from the adsorbate in the alimentary canal. It has been shown [46] that rats seriously depleted of vitamin B_1 cannot fully utilize the vitamin B_1 present in preparations such as fullers' earth adsorbates. In the curative method, therefore, the response to the international standard adsorbate does not represent the full vitamin B_1 activity of the dose given and the vitamin B_1 potency of the test substance determined by this method is accordingly judged to be higher than it really is. In the growth method, on the other hand, the animals are healthy and seem to utilize fully the vitamin B_1 of the standard adsorbate. Vitamin B_1 values by the growth method are therefore probably more nearly true values although considerably lower than those obtained by the curative technics.

Whether this same relationship holds for natural products depends on the availability of vitamin B_1 in these products.

Since the adoption of the international standards, attempts have been made to derive a factor for converting vitamin B_1 values expressed in Sherman units to equivalent values in international units. Values from 1 to 4 Sherman units equivalent to 1 international unit have been suggested. As explained in an earlier paper of this series,[47] the growth units have no fixed value in terms of the vitamin for which they are defined and therefore conversion factors cannot be derived accurately.

Many food products present a difficulty in vitamin B_1 assays not experienced so generally in the case of other vitamins. Although vitamin B_1 occurs in a wide variety of foods, the quantity present in most cases is small. This means that the test doses used in the biologic assays must be rather large and it is often difficult, if not well nigh impossible, to get the animals to consume enough of the allotted portions to make the test reliable. Furthermore, it may not be possible to obtain responses that are divergent enough to indicate the dose effect relation essential to the derivation of a true estimate of the potency of the test material.

The foregoing discussion is intended to imply that vitamin B_1 values that have been reported, especially those of unusual magnitude, should not be accepted categorically apart from a consideration of the method of assay used and the exactitude with which the values were derived from the results obtained. When using tabulated values expressed in international units it is advisable to scrutinize them carefully to ascertain whether they were determined experimentally in international units or were derived by the use of a conversion factor from values determined in terms of some other unit.

43. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 3, New York, Macmillan Company, 1926, p. 406.
44. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 5, New York, Macmillan Company, 1937, p. 395.
45. Roscoe, M. H.: The Distribution of the Vitamin B Complex: I. Leafy Vegetables, Biochem. J. **24**: 1754 (No. 6) 1930.
46. Keresztesy, J. C., and Sampson, W. L.: Utilization of Vitamin B_1 from Fullers' Earth Adsorbates, Proc. Soc. Exper. Biol. & Med. **36**: 686 (June) 1937.
47. Munsell, Hazel E.: Vitamin A: Methods of Assay and Food Sources, J. A. M. A. **111**: 245 (July 16) 1938.

CHEMICAL METHODS OF ANALYSIS

Although several chemical methods of analysis have been suggested for the determination of vitamin B_1, the thiochrome method is the only one that has been studied to any great extent. Early in 1935 Peters [48] reported that the purest preparations of vitamin B_1 available were converted by oxidation in aqueous solution into substances showing intense sky-blue fluorescence. Somewhat later, Barger, Bergel and Todd [49] succeeded in transforming vitamin B_1 into a pale yellow sulfur-containing compound by oxidizing it in alkaline solution with potassium ferricyanide. The compound formed showed an intense blue fluorescence in neutral or alkaline solution and had all the properties of the thiochrome described by Kuhn and his associates.[50] Jansen [51] studied the quantitative transformation of thiamin to thiochrome and concluded that the reaction took place at an optimal p_H of 10 and the maximum reaction in one or two minutes. Excess potassium ferricyanide seemed to destroy the thiochrome. The thiochrome was then extracted with isobutanol and the extract transferred to a Cohen fluorimeter. The test with the international standard was made by eluting the vitamin with a mixture of alkali and potassium ferricyanide. The procedure of alkali extraction was later adopted for removing the vitamin from other materials. Westenbrink and Goudsmit [52] applied the method of Jansen to the determination of vitamin B_1 in urine samples. The urine was diluted with three volumes of water and the reaction was carried out in an atmosphere of nitrogen. Errors due to interfering fluorescent substances were eliminated by "subtracting the fluorescence of a franconite eluate to which no potassium ferricyanide had been added from the fluorescence of some eluates which had been treated with different amounts of this oxidizing agent." Results by this technic agreed well with those obtained by Harris and Leong using the bradycardia method. Pyke [53] made a rather extensive study of the method as applied to the determination of vitamin B_1 in foods. The report covering this study gives a detailed description of the procedure, in which fluorescence was measured by a Cohen fluorimeter. Compensation for variation in intensity of the fluorimeter was obtained by reading the deflexion given by 10 cc. of solution containing 0.81 mg. of quinine sulfate in 100 cc. of tenth normal sulfuric acid. Readings from solutions of thiochrome were calculated back on the basis of 100 for this deflection. With the pure vitamin the fluorimeter readings and the concentrates of vitamin showed a straight line relationship. In the procedure as finally adopted the fluorescence given by a solution to which no potassium ferricyanide had been added was subtracted from the fluorescence of the treated solution to get that due to thiochrome. Karrer and Kubli [54] also give a detailed description of the thiochrome reaction. These investigators feel that the violet fluorescence of thiochrome can be estimated more advantageously by the eye than by a photoelectric fluorimeter. Hennessy and Cerecedo [55] report success in the elimination of nonspecific fluorescence by employing synthetic zeolites for absorbing the vitamin.

Several other tests suggested for vitamin B_1 also depend on the formation of colored compounds. Prebluda and McCollum [56] described a purplish red compound formed with vitamin B_1 and *p*-amino acetanilid or methyl-*p*-amino phenyl ketone treated with nitrous acid which was stable and highly insoluble in water. Naimans [57] found that with vitamin B_1 containing substances bismuth potassium iodide gives an orange red precipitate which can be filtered, dried and weighed. This reaction is specific for the thiazole nucleus and the weight of the precipitate is proportional to the quantity of vitamin B_1 present.

In 1926 Jansen and Donath claimed a strong Pauly reaction (red color when treated with diazotized sulfanilic acid in the presence of sodium carbonate) for crystalline preparations of vitamin B_1. This reaction was studied by Kinnersley and Peters,[58] who found that it was stabilized by the addition of formaldehyde. These investigators felt, however, that the specificity of the reaction needed further proof.

FOOD SOURCES

Vitamin B_1 has been shown to be present in a wide variety of foods, but there are few foods of plant or of animal origin that may be considered potent sources of this factor. In planning adequate diets, therefore, it is necessary to depend on several food items to furnish the day's supply of vitamin B_1. This is in direct contrast to experience with vitamin A and vitamin C, in which a single food may furnish the major portion of the requirement for the day. The problem of planning for vitamin B_1 is further complicated by the fact that it is desirable to insure an adequate supply in the diet each day, since vitamin B_1 is not stored in the body to any great extent. These considerations become more significant when viewed in the light of the current tendency to give more attention to the subacute and chronic forms of the deficiency diseases.

At the present time dietary calculations for vitamin B_1 are made difficult by the dearth of data on the occurrence of this factor in foods, as well as by the further fact that values expressed in terms of the rat growth unit still comprise the major portion of those available. It is to be hoped that the development of new methods of assay that are more specific and more precise will furnish the incentive for more extensive studies giving values in international units. Tables of numerical values are given in several textbooks, and a summary of data that appeared in the literature up to January 1936 will be found in a publication recently issued by the United States Department of Agriculture.[59] It seems

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49. Barger, G.; Bergel, F., and Todd, A. R.: A Crystalline Fluorescent Dehydrogenation Product from Vitamin B_1, Nature **136**: 259 (Aug. 17) 1935.

50. Kuhn, Richard; Wagner-Jauregg, Theodor; Van Klaveren, F. W., and Vetter, Hellmuth: Ueber einen gelben, schroefelhaltigen Farbstoff aus Hefe, Ztschr. f. physiol. Chem. **234**: 196, 1935.

51. Jansen, B. C. P.: A Chemical Determination of Aneurin (Vitamin B_1) by the Thiochrome Reaction, Rec. trav. chim. **55**: 1046, 1936.

52. Goudsmit, J., and Westenbrink, H. G. K.: Determination of Aneurin (Vitamin B_1) in Urine by the Thiochrome Method, Nature **139**: 1108 (June 26) 1937. Westenbrink, H. G. K., and Goudsmit, J.: The Determination of Aneurin (Vitamin B_1) in Urine by the Thiochrome Reaction, Rec. trav. chim. **56**: 803, 1937.

53. Pyke, M. A.: The Chemical Measurement of Vitamin B_1 in Foodstuffs and Biological Material by Means of the Thiochrome Reaction, Biochem. J. **31**: 1958 (Nov.) 1937.

54. Karrer, Walter, and Kubli, Ulrich: Zur Bestimmung von Vitamin B_1 (Aneurin), Helv. chim. acta. **20**: 369, 1937.

55. Hennessy, D. J., and Cerecedo, L. R.: The Use of Synthetic Zeolites in the Estimation of Vitamin B_1 by the Thiochrome Reaction, read before Division of Biological Chemistry, American Chemical Society, Dallas, Texas, during 1938.

56. Prebluda, H. J., and McCollum, E. V.: A Chemical Reagent for the Detection and Estimation of Vitamin B, Science **84**: 488, 1936.

57. Naimans, Barnet: A Reagent for Vitamin B_1, Science **85**: 290 (March 19) 1937.

58. Kinnersley, H. W., and Peters, R. A.: The Formaldehyde-Azo Test for Vitamin B_1, Biochem. J. **28**: 667 (No. 2) 1934.

59. Daniel, E. P., and Munsell, H. E.: Vitamin Content of Foods, Miscellaneous Publication 275, U. S. Department of Agriculture.

unnecessary, therefore, to consider here more than the general aspects of food sources of vitamin B_1 with particular reference to the precautionary measures essential to insure against unnecessary losses during manipulative procedures, such as cooking or canning.

Vegetables, including potatoes, may be regarded as forming one of the more important groups to be depended on regularly for vitamin B_1. Exclusive of legumes they may be considered for general purposes on a par with one another, since they do not show differences among themselves that make it feasible to group them for relative B_1 content on the basis of any particular physical characteristic such as color, for instance. Although fruits may be rated as only fair sources of vitamin B_1, they are important in that they are generally eaten raw and in relatively large quantities, if used at all.

Vitamin B_1 tends to be concentrated in the germ portion and outer or bran layer of seeds. Legumes, nuts and whole grains are among the good food sources. Refined cereals and flours, however, contain very little of the vitamin because the germ and the bran layer are largely removed during the refining process.

Eggs, muscle meats and, more especially, the organ meats are rated as good sources. These products are not subject to variation due to changes in the vitamin B_1 content of the diet of the animals from which they are derived, as is the case with vitamin A. Certain muscle meats, specifically chicken and pork, have been described as rather unusual sources when compared with other similar products. Whether this is actually the case or only an accident of assay should perhaps be left for further investigation.

Milk becomes an important source of vitamin B_1 when considered on the basis of the quantity usually consumed and the fact that it may be used without treatment that would tend to lessen its potency.

The foregoing statements should be taken as applying to untreated or fresh forms of the products described. They do not cover foods that have been subjected to any of the various manipulative procedures concerned in preserving the food or preparing it for consumption. Vitamin B_1 is inactivated by heat in the presence of moisture, but in foods at least it is not readily destroyed through oxidation.

The actual loss of vitamin B_1 during the heat treatment of food may or may not be significant, depending on the conditions that prevail. Under most conditions inactivation occurs gradually as the time or temperature, or both, of heating increases. For general purposes this need not be considered significant up to one hour at 100 C. The acidity (or alkalinity) of the medium, however, has a significant influence on the rate of destruction, since inactivation increases with decreasing acidity, especially at temperatures above the boiling point of water. Inactivation of vitamin B_1 in milk powder during dry heating in air at 100 C. for as long as forty-eight hours has been reported as small. Recent experience [60] indicates, however, that losses in foods under conditions comparable to those in baking may be as high as 50 per cent.

Although vitamin B_1 is not readily destroyed at the temperature of boiling water, the greatest loss due to cooking may take place in foods that are boiled. Vitamin B_1 is very soluble in water and it is easily conceivable that a large proportion of the vitamin may go into solution in the cooking water and be lost. Unless this liquid is served in some way to the person eating the food, the food itself should be held a questionable source of vitamin B_1, even though in the untreated form it is rated as a good source. This illustrates a cardinal point that unfortunately is often overlooked, namely that it is not the inclusion of a food item in the diet that is important but its actual nutritive value when consumed.

During canning of foods there is probably little loss of vitamin B_1 due to processing per se. Any loss noted in such products probably took place during the preparation of the food prior to the time it was put in the can. The full vitamin B_1 value of canned products is obtained only if no portion of the contents is discarded.

Too few data are available on the effect of storage on the vitamin B_1 in foods to admit of any definite generalization in this regard. There is little reason for believing, however, that there is any significant loss of vitamin B_1 under storage conditions that preserve the food satisfactorily for consumption. Information on the effect of drying is also scanty. The foods that have been assayed in the dried state were, for the most part, dried to reduce the bulk of the sample so that the experimental animal would consume the portion allotted. The material was dried under conditions assumed to effect no loss of vitamin B_1. This was only an assumption, however, since check tests could not be made on comparable samples of the fresh product. Results of assays carried out in this way have little significance, therefore, in relation to the vitamin B_1 content of the fresh product. Milk may be cited as an exception, since studies designed to determine losses of vitamin B_1 during procedures used to reduce the water content have been made on comparable samples of the fresh and dehydrated or partially dehydrated product. Losses during evaporation and drying were shown to be small.

Freezing seems to be a satisfactory method of preserving the maximum nutritive value of foods and there is reason to believe that vitamin B_1 is preserved in stored frozen foods, as well as are the other vitamins. When frozen foods are cooked, it is essential to remember that the vitamin may be more easily extracted from these than it is from the fresh product, and that care must be taken to serve all expressed juices.

Although it is permissible to claim that the ordinary diet may easily contain adequate supplies of vitamin B_1, it seems advisable to suggest that there is an almost equal opportunity for it to be low in this factor. The tendency to replace whole grain products by refined cereals and flour may entirely eliminate this important source for many individuals. Vegetables are often cooked with little or no regard for loss of vitamin B_1 value or, for that matter, nutrients of any sort. These two indiscretions alone eliminate two of the chief sources of this vitamin. Fruits, meat, milk and eggs, which constitute good sources of vitamin B_1, are among the high cost foods and are the first to be omitted in the low cost diet. With these considerations in mind it would seem to be expedient to give more attention to the vitamin B_1 supply especially in certain types of diets and to the possible ill effects that may result from the long-continued use of a diet low in this nutritionally important factor.

60. Unpublished data, Bureau of Home Economics, U. S. Department of Agriculture.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

ILLE PORTABLE UNDERWATER THERAPY TANK ACCEPTABLE

Manufacturer: Ille Electric Corporation, 386 Fourth Avenue, New York.

The Ille Portable Underwater Therapy Tank with Hydro-Massage is essentially a portable whirlpool bath recommended for heat treatment of legs and arms. It is designed for use in hospitals or offices. The complete equipment includes an extra wide stainless steel tank with an adjustable canvas seat, turbine agitator, immersion heater with dial thermometer and pump, all electrically operated, and filling hose, an arm rest, and optional metal chair on high frame for use in leg treatments. The tank rests on a heavy metal base mounted on four solid rubber casters for ease in moving from place to place. Total shipping weight is approximately 350 pounds or 325 pounds without chair. Inside dimensions are 28 inches high by 16 inches wide by 36 inches long. It operates on alternating current. Special equipment is required for direct current.

Ille Portable Underwater Therapy Tank.

It is filled with water by means of a hose which fits over any available standard faucet. Once filled, the tub may be trundled wherever the operator desires. The water is agitated and aerated by an electric turbine type of pump. The water is maintained at the desired temperature level by the immersion heater (1,000 watt consumption). The dial thermometer permits continuous reading of the temperature.

The agitator produces a gentle hydromassage, which is applied most effectively by placing the underwater jet next to the affected part. A gear device and crank enable the operator to move the agitator up and down within the tub and to increase or decrease the velocity of the ejection. The motor driven agitator may be attached to a full size tank large enough to permit the patient to lie at full length. Such tanks may be purchased from the manufacturer.

There is an electric pump for draining the tank. A valve connected to the lower part of the drain pipe permits complete drainage of residue.

This unit was investigated clinically and found to produce therapeutic effects not unlike those produced by other whirlpool baths. Mechanically it appears to be a well made piece of equipment.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Ille Portable Underwater Therapy Tank for inclusion in its list of accepted apparatus.

ADLANCO W-73 TWO-TUBE ULTRATHERM NOT ACCEPTABLE

Manufacturer: Adlanco X-Ray Corporation, 54 Lafayette Street, New York.

The Adlanco W-73 Ultratherm is intended solely for medical use. It is similar to the Council accepted Model G Ultratherm (THE JOURNAL, Nov. 14, 1936, p. 1636) except for a certain difference in wiring owing to the use of two tubes in place of one. The cabinet model may be procured with a walnut finish or a white painted exterior. Glass insulated electrodes are attached to the machine by rigid electrode arms with movable joints.

The unit contains two vacuum tubes, rated at 250 watts each. Its circuit is of the push-pull type. There are two transformers —one high tension, supplying current to the anodes, and one low tension, supplying current to the filaments of the tubes. The high tension current is controlled by a five step switch. The filament current is controlled by a three step switch, supplying power with a voltage subject to local variations.

The output was measured by a lamp load, photoelectric cell and wattmeter. Six carbon filament lamps, each with 100 watt capacity, were connected in parallel and the maximum power output was determined to be 495 watts. The line electromotive force was 111 volts. Input power under these conditions was 1,460 watts.

The transformer temperature rise, taken after a two hour run at full load, was within the limits of safety. Burns may be procured with this unit but may be avoided by employing ordinary precautions. Provision has been made to eliminate radio interference by insertion of line filters.

The unit was investigated in a clinic acceptable to the Council and rendered satisfactory service. It appears to be as efficient as the average device of this type. No evidence was submitted by the firm to substantiate the efficacy of the unit in heating the deep muscle tissues of the living human thigh, although such information was requested and ample time given to obtain these data.

Since the firm has not fulfilled the requirements for acceptance and has circulated advertising matter which contains misleading, unwarranted or exaggerated statements, the Council voted not to accept the Adlanco W-73 Two-Tube Ultratherm for inclusion in its list of accepted devices. However, the Council will give the unit reconsideration without prejudice when the requirements and the Official Rules have been met.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

MRS. PALEY'S BABY FOOD—STRAINED GREEN BEANS

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Canned, cooked sieved beans slightly seasoned with salt.

Manufacture.—Fresh green beans are thoroughly washed, trimmed, pressure cooked, sieved, filled into glass jars, vacuum sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 92.2%, total solids 7.7%, ash 0.5%, fat (ether extract) 1.1%, protein (N × 6.25) 1.4%, reducing sugars as dextrose 1.4%, crude fiber 0.5%, total carbohydrates other than crude fiber (by difference) 4.4%, calcium (Ca) 0.040%, phosphorus (P) 0.028%, iron (Fe) 0.002%.

Calories.—0.3 per gram; 9 per ounce.

NUTRADIET BRAND UNDILUTED GRAPEFRUIT JUICE

Distributor.—The Nutradiet Company, a subsidiary of S & W Fine Foods, Inc., San Francisco.

Description.—Canned Florida grapefruit juice packed without added sugar.

Manufacture.—Tree-ripened grapefruit is mechanically cleaned and washed, cut in halves and reamed. The juice is strained, automatically filled into cans, vacuum sealed and processed at 71 C. for five minutes.

Analysis (submitted by manufacturer).—Moisture 87.7%, total solids 12.3%, ash 0.4%, fat (ether extract) 0.06%, protein (N × 6.25) 0.6%, crude fiber 0.03%, carbohydrates other than crude fiber (by difference) 9.5%, titratable acidity as citric acid 1.7%, vitamin C (dye titration) 0.48 mg. per gram.

Calories.—0.41 per gram; 12 per ounce.

Vitamins.—Approximately 275 international units of vitamin C per ounce.

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SATURDAY, SEPTEMBER 3, 1938

SPECIAL SESSION OF THE HOUSE OF DELEGATES TO CONSIDER NATIONAL HEALTH PROGRAM

The House of Delegates is the only body authorized under the Constitution and By-Laws of the American Medical Association to establish policies for the organization. Contrary to general belief, neither the Board of Trustees, the president nor any of the other officers or employees of the Association can establish a policy or point of view for the Association. It is their duty, once policies have been established by the House of Delegates, to promote and enforce them.

Ordinarily the House of Delegates meets once each year at the time of the annual session; the policies there promulgated become effective and remain effective until changed at a later session. To maintain the flexibility of the organization, however, the By-Laws provide that a special session of the House of Delegates may be held in response to a call issued by the speaker of the House whenever a sufficient number of members of the House of Delegates or of the Board of Trustees deem such a special session necessary. Some years ago when the Social Security Act was under consideration a special session of the House of Delegates was called to consider the part to be played by the American medical profession in this legislation. Now the Association is confronted with a national health program of tremendous scope and with the statement that it is the intention of the federal administration to make this program effective by legislation to be introduced at the next session of the Congress.

The Board of Trustees, having given this matter serious consideration, determined to request the speaker of the House of Delegates, Dr. H. H. Shoulders, to issue a call for the convening of a special session of the House of Delegates for this purpose. This call has been issued and the meeting will take place in Chicago on September 16. According to the announcement of the speaker:

> The business to be transacted at this special session shall be limited to the consideration of the national health program submitted to the National Health Conference recently held in Washington and to such other matters as may be submitted to the House of Delegates by the Board of Trustees.

The American Medical Association is among the most democratic organizations in the world today. Members of the House of Delegates are chosen by the houses of delegates of the individual state and territorial medical societies and these, in turn, are composed of delegates sent by the individual county medical societies. Such policies as the House may establish will become the official policies of the Association, to be urged on the medical profession, on the government and on the public generally as the House of Delegates may direct. Members of the American Medical Association will do well to follow closely the deliberations of this special session. Once the House of Delegates has spoken, its actions should be supported by the united voice of American medicine, so that it may be heard with respect and consideration when legislation comes before the Congress of our country.

THE EXPANDING INTEREST IN INDUSTRIAL HEALTH

Industrial health as a field of special medical interest is young. Its origin, first strivings and subsequent development are well within the memory of many physicians today. Indeed, many pioneers who early foresaw the notable contributions which medicine could make toward improving the physical and environmental welfare of American industrial employees are active today. Except by a devoted few, little serious attention was given to safe and healthful practices in industry thirty years ago. Few physicians realized the preventable character of most occupational disorders. By 1910, however, the preliminary investigations of the principle of compensation for industrial injuries had prepared the way for implementing the recommendations of the fact-finding commissions. The subsequent rapid and widespread adoption of compensation legislation by the states began to exert a profound influence on medical thought and practice. The forward-looking element in industry and in the medical profession recognized that a health and safety program, as adequate as possible within the limits of time and available personnel, was a necessity not from motives of altruism but as sound business practice.

Demands on the medical profession in the field of industrial health have continued increasingly. The interest which was formerly concentrated on traumatic and reconstructive surgery has expanded immeasurably.

At present there is scarcely a field of medical practice which has not been affected by problems of industrial health or has not contributed toward their solution. The strictly preventive medical aspects have long been preeminent in the scientific attack on occupational hazards. The achievements of the Division of Industrial Hygiene and Sanitation of the United States Public Health Service over the past twenty-five years have recently resulted in the establishment of similar agencies in the health departments of many states and some cities. In 1915 the Section on Preventive Medicine and Public Health of the American Medical Association conducted a symposium on industrial sanitation; in every succeeding meeting similar material has been presented.

Realization of the expansion of interest in industrial medicine led the House of Delegates of the American Medical Association to create the Council on Industrial Health. Correspondence on specific professional problems in industrial medicine has steadily increased and the space which has been assigned to this subject in THE JOURNAL has become greater and greater. Indeed, all the councils and bureaus of the Association are cooperating in the aid of physicians who need assistance in meeting the problems of adequate industrial medical care.

The record of achievement is gratifying to all who have contributed toward the elevation of standards and practice in industrial health. As in the case of workmen's compensation, the solution of some problems has only served to demonstrate the presence of others. The necessity for continued concentration on and devotion to the contribution which medicine can make to minimize the ill effects which occupation and working conditions may have on the health and well-being of the individual worker is apparent.

METAPLASTIC IMMUNITY

According to MacNider [1] of the University of North Carolina, there are variations in the resistance of individual tissue cells to toxic agents. As a result of this variation less resistant cells are killed by the properly graded dose of toxins, selective hypertrophy or regeneration of the relatively resistant remaining cells rendering the organ or tissue relatively immune to this toxin. His earliest demonstration of this "metaplastic" immunity was a study of acquired uranium tolerance in the kidneys. Following the subcutaneous injection of 2 mg. of uranium nitrate per kilogram of body weight, acute nephritis invariably develops in normal dogs. The kidneys of these dogs show degenerative changes, particularly in the tubular epithelium. A second injection of uranium nitrate made before full functional recovery invariably increases the severity of this epithelial degeneration. If the second injection is delayed, however, till the animals have established complete functional regeneration, it is usually found that the dogs are relatively immune to uranium nitrate, 4 mg. per kilogram of body weight producing no nephrotoxic symptoms. A similar acquired tolerance to uranium in the kidney was subsequently demonstrated in rabbits.

Histologic studies of the kidney immune to uranium show a "metaplastic" repair, replacement of the lost tubular epithelium with cells of a syncytial type. This regeneration can be conveniently classified as a survival and regeneration of the "fittest" or "metaplasia," although the latter word is open to criticism.

Following his initial demonstration of metaplastic immunity in the kidneys, MacNider demonstrated similar syncytial regenerations in the liver. Following the subcutaneous injection of a dose of uranic nitrate sufficient to cause metaplastic regeneration, the animals acquired a tolerance to uranium accompanied by a tolerance to various other hepatotoxic agents, including chloroform. Studies of dogs in which this syncytial type of hepatic regeneration had been produced many months previously showed that the acquired hepatotoxic tolerance can persist for at least four years. Focal reversions of the liver cells to the earlier chloroform susceptible types, however, were occasionally demonstrable.

That metaplastic regeneration actually takes place in animals maintained under normal conditions is shown by MacNider's study of eighteen senile dogs. Thirteen of these dogs showed a normal liver function as far as could be determined by the phenoltetrachlorphthalein test. These animals, however, were completely resistant to a normally necrotizing dose of chloroform. Histologic study showed numerous syncytial cells in the liver.

Thus far, immunologic theorists have shown but slight interest in MacNider's concept because his work has been limited to highly specialized parenchymatous tissues. If a similar selective regeneration can be shown to be operative in the spleen, bone marrow and other parts of the reticulo-endothelial system, however, his metaplastic theory may form the basis for some future theory of specific antibody production. Recent studies of in vitro production of specific antibodies by splenic fragments seem to be in accord with his theory. Only after splenic tissues have recovered or regenerated from specific antigenic assault do they have the power to produce corresponding antibodies in vitro.[2] Whether or not this "preparedness" is due to selective regeneration or to metaplastic proliferation, however, has not yet been determined.

1. MacNider, W. deB.: J. Pharmacol. & Exper. Therap. **56**: 359, 373, 383 (March) 1936.

2. Tissue Preparedness for the Production of Specific Antibodies, editorial, J. A. M. A. **110**: 2156 (June 25) 1938.

Current Comment

"YOUR HEALTH" ON THE AIR AGAIN

Beginning October 19 and for thirty-six weeks thereafter the American Medical Association and the National Broadcasting Company will again unite in offering the American people the radio feature Your Health. Details as to date, time and topics will be found either under Association News or in the Organization Section of THE JOURNAL and monthly in a radio department supplementary to the programs in *Hygeia*. This radio program, which received the First Award in its classification from the ninth annual conference of the Institute for Education by Radio,[1] thus enters its fourth year of dramatic presentation, its sixth year of continuous fall, winter and spring broadcasting and its second year in a form designed specifically for supplementary use in connection with health teaching in the schools. The program has been used for health teaching by the schools in New York, Chicago and numerous other cities in all parts of the United States. Comments relative to it have been received from the British Isles, where it has been heard through short wave broadcasting. It is based on the conception that health teaching can be enriched and its value enhanced by presentation of health situations in interesting and amusing dramatic form with appropriate musical interpolation, all presented under the experienced direction and by the able artists of the staff of the National Broadcasting Company. The ultimate usefulness of such a program depends on its local reception. All that the American Medical Association and the National Broadcasting Company can do is to put the program on the network. To be effective, it must be broadcast by as many as possible of the local stations affiliated with the network; of these only a few are owned and operated by the National Broadcasting Company and only over these has the network any control. All other stations affiliated with the network may broadcast the program Your Health locally or they may not. Their decision depends largely on whether or not revenue-producing local programs are available at the same time. In many instances when the program Your Health has not been broadcast it has been because of previous commercial commitments. Therefore local medical societies and auxiliaries should make immediate contact with the managers or program directors of the local stations on the Blue network of the National Broadcasting Company as listed on page 945 of this issue of THE JOURNAL and inform them as to the character of the program Your Health and the day and hour when it will be on the network. In most instances radio stations are eager to use good educational broadcasts if they learn about them in time to avoid conflicts with revenue-producing features, which latter obviously the station must have if it is to pay its expenses. In some instances when commercial commitments already have been made it may be possible by conferring with the commercial sponsor to effect a change of schedule satisfactory to all concerned which will permit the local broadcasting of the program Your Health.

1. Award to American Medical Association Radio Program, Current Comment, J. A. M. A. **111**: 160 (July 9) 1938.

DEATHS FOLLOWING ELIXIR OF SULFANILAMIDE-MASSENGILL: VII

On November 6, 1937, THE JOURNAL published a special report under the auspices of the A. M. A. Chemical Laboratory dealing with the chemical composition of elixir of sulfanilamide-Massengill, pharmacologic work reporting results following the administration of elixir of sulfanilamide-Massengill, and pathologic studies on the necropsy material from both animals and man. In addition there was a map indicating where the deaths had occurred. The pharmacologic and pathologic reports by Drs. Geiling and Cannon indicated that further investigations were under way. The preliminary investigation showed that there was no essential difference in the results whether elixir of sulfanilamide-Massengill in the doses recommended or comparable doses of a "synthetic" mixture or of diethylene glycol were administered. In the more extensive work by Geiling and Cannon (reported elsewhere in this issue [1]) these conclusions have been confirmed. In addition the authors have had an opportunity to study the possible mechanism of the action of the elixir and of diethylene glycol alone. They again report that the pathologic picture is essentially similar in the different species of animals when given the three preparations containing diethylene glycol that have been enumerated; that the pathologic changes were apparently those of a severe chemical nephrosis with intracellular edema of the epithelial cells of the convoluted tubules resulting in tubular obstruction by compression and by the intraluminal formation of casts. This intracellular edema in the kidneys leads to internal disorientation of cells of the convoluted tubules and offers an explanation for the tubular obstruction, anuria, uremia and death. Whether this intracellular change is due to cellular anoxia or whether it is due to hygroscopic properties of diethylene glycol are questions needing further investigation. In analyzing the composite clinical picture they bring out that there was apparently considerable variation in the responsiveness of patients to elixir of sulfanilamide-Massengill. They examined tissues of fifteen persons who died following the use of the diethylene glycol-containing elixir. Their observations coincided essentially with those reported by Drs. I. A. Nelson and H. A. Ruprecht and by Dr. Hagebusch as well as by a number of others.[2] Evidently the time interval between doses and the concentration in which the elixir was recommended for human use exceeded the capacity of the body to handle the drug without producing serious injury. The pharmacologic staff of the Food and Drug administration at Washington is conducting experiments which according to unpublished reports are in general accord with the observations reported by Drs. Geiling and Cannon.

1. Geiling, E. M. K., and Cannon, P. R.: Pathologic Effects of Elixir of Sulfanilamide (Diethylene Glycol) Poisoning, A Clinical and Experimental Correlation, Final Report, this issue, p. 919.

2. Drs. Harry C. Schmeisser, T. C. Moss, C. E. Gillespie and K. M. Lynch have reported similar results.

ORGANIZATION SECTION

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

REPORT FROM ROCK COUNTY, WISCONSIN

The study of need and supply of medical care inaugurated last February [1] by the American Medical Association through its state and county medical societies is progressing. Study forms and instructions to assist state and county medical societies in the study of medical care have been sent on request to forty-three states and the District of Columbia.

Several county medical societies have already finished their local studies of the need and supply of medical care and have sent completed summary sheets and reports of findings and recommendations to the Bureau of Medical Economics. Following are the results of the study made by the county medical society of Rock County, Wis. Other reports will be published from time to time.

ROCK COUNTY, WISCONSIN

Rock County covers an area of 716 square miles in the extreme southern portion of Wisconsin. The county forms part of the Illinois-Wisconsin state line, approximately midway between Lake Michigan and the Mississippi River, and lies in a manufacturing and dairying district. According to the 1930 census the population of Rock County was 74,206. The two main population centers are the cities of Beloit, with a population of 23,661, and Janesville, with 21,628 persons. A total of 30,041 persons were gainfully employed in 1930: 12,719 in manufacturing industries, 11,765 in trade, service and other nonmanufacturing industries, and 5,557 in agriculture.

In economic status Rock County ranks seventh of the seventy-one counties in Wisconsin, according to the Wisconsin Regional Planning Committee. This ranking is based on weights given to factors such as per capita income, percentage of population on relief, employment, occupational trends and health. However, with regard to health, as measured by birth and death rates in relation to average birth and death rates for the state, Rock County was ranked forty-eighth.

The study of medical care in Rock County was conducted under the auspices of the Rock County Medical Society by the board of trustees, Drs. G. W. Belting president, C. R. Gilbertson vice president, O. W. Friske secretary, Wayne A. Munn, H. E. Kasten, W. T. Clark, F. Van Kirk and W. O. Thomas. By seeking the cooperation of all individuals and organizations concerned with medical care in Rock County, such as physicians, dentists, nurses, pharmacists, hospitals, health departments, welfare and relief agencies, schools, colleges and other organizations, this study committee determined the supply of and the need for medical services in Rock County, as follows:

An inventory of the medical services and facilities was made which revealed that there are 102 physicians: eighty-eight in active practice, three in administrative positions, and eleven retired or not in practice; sixty dentists; fifty-two full time and ten part time private duty nurses and four full time and two part time public health and visiting nurses available for nursing care of the sick in their homes; five hospitals: three general hospitals with a bed capacity of 218, one tuberculosis hospital with sixty-eight beds and one mental hospital with 330 beds; thirty-five pharmacists; four clinics—two operated by the health departments and two by welfare and relief agencies—providing for general medicine and surgery, maternal and child welfare, eye, ear, nose and throat, nervous and mental, venereal disease, tuberculosis and dental patients; seven health departments; one private and two government agencies which arrange for or provide services such as care in physician's or dentist's office, medical care in the home, hospitalization, drugs, eyeglasses and surgical appliances; twenty schools below the college level providing health supervision services for pupils; one college with a student health service, and seven other organizations such as mutual benefit associations and fraternal orders which arrange for or provide medical services.

Such a matter of fact inventory served a useful purpose by indicating the nature and extent of the agencies through which medical services are made available to the residents of Rock County. For example, there is a physician in active practice for every 843 persons in Rock County, which is fewer persons per physician in practice than the average for the United States. No person in the county would have to travel farther than fifteen miles to reach a physician. During 1937 general hospital beds in private rooms were 76 per cent occupied, in semiprivate rooms 55 per cent and in wards 63 per cent, indicating that general hospital beds are fairly well distributed according to room accommodations and that the number of such beds seems more than adequate. The daily room rates charged, $2.50-$3 for a ward, $3-$4 for semiprivate and $4.30-$6 for private accommodations, are not excessive.

The question of availability of medical services for indigents and for low income persons was investigated fully. More than 3,000 persons received free medical service direct from physicians and dentists in the office, home or hospital. Over 500 patients received hospital care, free or at public expense, from hospitals within the county, in addition to some 200 patients sent at public expense to the Wisconsin General Hospital in Madison. More than 27,000 days of hospital care were provided at no expense to the patients. Nursing visits made without charge to patients numbered more than 4,500. Eighteen pharmacists compounded 390 prescriptions without charge and 5,954 prescriptions at cost or reduced fees.

Information obtained from all sources indicates that medical services are readily available in Rock County. The health department, with thirty requests for medical care, reported no difficulty in obtaining such care. Of 162 persons reported to the health department as in

1. J. A. M. A. **110**: 77B (Feb. 12), 127B (March 5) 1938.

need of medical care which they were not receiving, the causes were unemployment or inadequate income and a lack of knowledge of the procedure for obtaining medical care. Approximately one fourth of these persons did not desire medical care because of indifference or unwillingness to cooperate with any social agency.

COMMENTS ON THE NEED FOR MEDICAL CARE

Some comments on the need for medical care were as follows:

From physicians:

There is no one in Rock County who cannot secure medical, dental or hospital service. Every one can secure aid, unless they are too lazy to come and see a doctor. Our outdoor relief takes care of any one that is indigent for any reasonable illness; the only thing excepted is chronic pelvis relaxations, hernias, and things not causing acute trouble. There are some borderline deadbeats who drink up all of their money that do have trouble routing out a doctor at night, but the next day they can secure aid at the hospital for any acute illness. The family welfare, visiting nurse association, and all agencies bring these people to the doctor.

I have found no cases in which a patient was refused care because he was unable to pay. I have found many cases referred by agencies such as the Family Welfare, Crippled Children's Association, the Police Department, Municipal Hospital, where the doctor's services were expected gratis and no attempt was made by those organizations to secure compensation for the physician. I have found several cases where payment for adequate care of the patient has been refused by the relief agencies but has been carried out at his own expense by the physician.

It is my belief that in Rock County there is no need for medical services that is not supplied by the County Welfare Department, the health departments of the county and cities, and private welfare agencies as well as those supplied by the County Judge under the state law. The public welfare department not only supplies necessary medical care but such care as may seem indicated to prevent possible disability and dependency in the future such as removal of tonsils and infected teeth. Glasses are supplied to school children who need them and also to adults whose defective vision may incapacitate them for doing their regular work or who if supplied glasses could be put to work. Hernias are treated with trusses or if the individual is young and would be taken into private employment after operation, operation is authorized. In other words, medical service meets not only emergency needs but has been placed on a constructive social basis with the idea of returning disabled persons to useful employment. Strict supervision is kept over all medical services rendered to the end that unnecessary medical expense is not authorized and the cost to the community is kept within reasonable bounds. Consideration is given to all elements of society in an effort to be fair to the patient, the taxpayer, and the physician.

From dentists:

I believe the present system used in Rock County is very good, efficient, and fair to the profession and the public.

The local relief takes care of the operative cases needing extraction, but otherwise persons do not get the work they should have done, such as just ordinary extractions where no local or systemic reaction is noted; and practically no restorative work is allowed on any except minors and many are in need.

People who are not being treated have every opportunity to receive dental care so far as I know—either through the county setup or by private dentist.

From a hospital superintendent:

All of the hospitals of the county are of the opinion that the people are receiving adequate medical care through the relief setup. They, however, deplore the fact that the county is unable to pay only such a small fee as is stipulated in their contract. It is the general feeling of the supervisors of hospitals that relief patients in general receive much better care than the borderline type of individuals.

From health officers:

In Beloit any one who wants to be vaccinated, have shots for diphtheria or a tuberculin test can get it free of charge and is urged to do so. Indigents requiring medical care can easily get whatever they require through the Relief Office. I believe the problem here is how to get hospital care and laboratory and x-ray work for self-supporting people of the low income group.

From my observation, there are many adults and children who very badly need medical care. Many of them insist they are unable to pay current medical fees. One or two have bitterly criticized these as being too high. Many families needing care do not appreciate its value and it would seem that only through much more education of the general public can this attitude be changed.

From pharmacists:

We have very good facilities for the needy to get aid under our existing county aid and city health office. If people properly apply, they will be taken care of and so far we have had no complaints, and I wish to comment on the policy that the patients have their choice of the doctor, and the doctor has freedom to prescribe what he knows best for their individual needs, not being limited or restricted in a real humane cause.

The patients on county relief do not hesitate to call a physician and probably get more medical attention than the average individual who has to pay for services. The above statement does not infer that they receive better service; it only means they receive more in proportion. The present system is much preferred to having only two or three physicians in the whole county take care of these people. We do not receive a fair remuneration for our services, so we accept what is forced upon us.

RESPONSIBILITY OF LOCAL AUTHORITIES

The development of the present arrangement for the care of indigents in Rock County illustrates the struggle that is often necessary to get local authorities to recognize their responsibilities to the indigent sick. Prior to 1932 the indigent sick in Rock County were cared for by two physicians hired by the county board on a part time basis. The operation of this arrangement is described as follows:

Each physician received $100 a month, plus allowances for drugs and for obstetrical cases over and above a minimum which was stipulated in the contract. This system was very unwieldly and the county physician was completely "swamped" with work, patients frequently having to wait several days for an appointment to see the county doctor. Every one was dissatisfied because they were forced to accept the services of a certain physician whether they liked him or not, and obviously this man could not render effective service to the great number of people he was expected to care for.

Additional funds for the medical care of the indigent sick could not be obtained, so the Rock County Medical Society created "Cooperative Medical Clinics, Inc.," to operate two clinics for indigents with all services donated by physicians. Drugs and hospitalization could be obtained in an emergency case. By February 1933 the families on poor relief had increased to 3,143 and the burden of free medical care was becoming too heavy for physicians to carry. A committee from the medical society secured a temporary agreement with the Rock County Board of Supervisors whereby certain patients who could not be cared for by the county physician could receive care from other physicians, who would be paid 50 per cent of regular minimum fees.

Finally the members of the Rock County Medical Society concluded that it was no longer possible for

physicians to carry the ever increasing load of medical care for relief persons, and the following resolution was passed:

WHEREAS, The care of the indigent is properly and legally a government function; and

WHEREAS, Medical, dental, surgical and hospital care is specifically mentioned in the laws of the state along with food, clothing, heat and shelter as necessities which must be furnished the indigent; and

WHEREAS, The medical and dental professions have for a great many years carried an unfair proportion of relief work along this line; and

WHEREAS, The situation is such that we can no longer continue to do this work gratis; and

WHEREAS, The care of the indigent is a county responsibility and the failure of the county to assume its obligation operates to deny the larger group of citizens who are striving to maintain an independent status in life the lesser rates which physicians would receive in the event that they did not have to carry the complete load of the indigent; therefore, be it

Resolved, That the members of the Rock County Medical Society, and the Rock County Dental Society in special meeting assembled, go on record that they can no longer gratuitously care for the indigent.

A committee was then appointed to meet with the county board of supervisors, and after many stormy sessions an agreement was reached whereby indigent persons were to have free choice of physician. The physician would receive 50 per cent of his regular minimum fee. Hospitals were to provide hospital care at a minimum rate of $17 weekly plus certain extras provided in the fee schedule, and pharmacists were allowed 20 per cent above cost for drugs and medical supplies. A description of the operation of this agreement for the care of the indigent is given as follows:

A physician is given an order to care for an indigent patient by the Rock County Relief Department. Attached to this order is a double postcard upon which the patient's physician must make an immediate report and an estimate of the number of visits or the type of medical work which the patient requires. All indigent patients have an absolute choice of physician and may get a relief order to see any one they wish. The only restriction being placed upon them is that they must keep the doctor they choose for at least one month and cannot change doctors until the following month unless for very urgent reasons. In case of surgical work or any extended illness, the consultant for the county board must see the patient before any expense is involved to determine the necessity for special care. The Committee on the Care of the Indigent [consisting of four physicians appointed by the medical society] meets on the first Tuesday of every month to audit all bills presented for the indigent.

The Relief Department makes an investigation of the financial and social history of patients in order to determine whether or not their income justifies public assistance. General hospitals do not maintain charity wards, and every one is expected to pay unless authorized as eligible for public assistance by the Relief Department; nevertheless, as has been indicated, many patients receive free services in the hospital. Nursing organizations are reported to follow no definite procedure in determining inability of patients to pay. Also, as has been indicated, physicians render services at greatly reduced fees for persons on relief and free services to thousands of their own patients in addition to the hours of service spent in clinics. Indigent tuberculous patients are given free hospitalization in a county sanatorium. A county institution for the care of the aged and the chronically insane is also maintained which furnishes medical and surgical services for inmates at county expense.

ATTITUDES TOWARD ARRANGEMENTS FOR CARE OF INDIGENT SICK

The attitude toward the present arrangements for the care of the indigent sick was expressed as follows:

It was unanimously concluded that, as far as the indigent of Rock County are concerned, this phase of the care of the sick no longer presents a problem. All indigent in this community are excellently cared for as is every one who might have any possible claim upon governmental facilities for assistance in his sickness care.

The success of the arrangement for the care of the indigent has made it possible for the medical society to secure the approval of the county board for the formation of a county sanitary unit consisting of a health officer and a sanitarian. This proposal was previously turned down by the county board.

The problem of hospitalization for indigents has a special aspect in Wisconsin because of the existence of a state law which makes it mandatory on the county judge to send a patient to the Wisconsin General Hospital in Madison if the patient selects that institution. Under this law each county is given a quota of patients who may be sent to the Wisconsin General Hospital and for whom the state will bear one half of the expense and the county the other half. Consequently, Rock County must pay $2.10 a day for all patients within a quota of 128 who select the Wisconsin General Hospital and $4.20 a day for those patients who exceed the quota. The Study Committee felt rather strongly that this law should be changed so that the indigent patients may be hospitalized at home. Their attitude is expressed as follows:

Briefly, our County Judge has spent $24,000 for the hospitalization of cases in the Wisconsin General Hospital during the past year, taking care of only 232 cases, while the Rock County Medical Society in its setup with the Rock County Welfare Department has hospitalized 271 patients, paid the doctors and furnished postoperative care and drugs at home for only $17,590. The total cost of office, home care, obstetrical, and everything for the thousands of patients cared for by our Relief Department during the last fiscal year was only $37,000. This seemed to prove to the Board of Trustees that the pernicious practice of sending patients out of the county and increasing the tax burden would have to stop. . . .

We feel we can do a better job more cheaply in our local institutions than can be done on the ordinary routine cases which are being sent away. It will always be necessary to send certain complicated cases which are especially suitable for teaching purposes to the Wisconsin General Hospital, but it is felt that the great majority of the indigent should be taken care of with our own county facilities. . . .

The Study Committee also advises the substitution of a medical committee in each county of the state for the services now performed by the county judge, this committee to have full power to determine whether or not it is necessary to send a patient to the state institution or whether there are ample facilities in the county to care for the individual. It is felt that this arrangement would be more fair to the patient, the physician, and the taxpayers of the county.

It is also pointed out that there are two distinct agencies—the relief department on the one hand and the county court on the other—handling medical relief. This, it is said, causes dissatisfaction, as each agency operates under a different statutory definition of eligibility for relief and it often happens that a patient may be denied medical aid through the county relief office and still be entitled to assistance from the county court.

CARE OF BORDERLINE PATIENTS

The problem of caring for borderline patients was given special attention. This problem was outlined as follows:

In an industrial community such as is reported by Beloit and Janesville, about 60 per cent of the total population may be classed as borderline patients in such times as we are just now experiencing. With the various shops working only two and three days a week, the average pay check has been more than cut in half, and we have a great number of people who do not have anything left with which to pay for medical services.

There are literally thousands of people in this county who are attempting to maintain an independent status in life who are too proud to go to any doctor and ask for help when they are confident that they will have no funds available in the near future to make even moderate payments for their medical services. As a result of this situation, thousands of people are neglecting their teeth while dentists offices remain empty, and very little reconstructive work on the teeth is being done. This summer, especially, people seem to be neglecting their children's tonsils because they can see no way in which they can pay even a minimum charge of $25 for such work. It is obvious that hundreds of women are neglecting to care for cervical erosions and lacerations, and minor gynecological complaints, which are the precursors of cancer if long neglected. There are also hundreds of men in this county who are suffering from hernias of various types and who have no hope of having this condition corrected by surgery. It would be utterly impossible for them to take six weeks away from their work and then to be a semi-invalid for a couple of months longer in order to get a cure for their hernia. They cannot afford to be away from their occupation for this length of time, to say nothing of paying a large hospital and medical bill which would be involved. . . .

We feel that some plan should be adopted whereby the large group of borderline patients can secure laboratory, x-ray and hospital facilities on a prepayment basis. This will greatly aid the physician because at the present time there are very few of these individuals who can avail themselves of diagnostic facilities, and consequently the doctor must do the best he can in treating these patients in his office without the aid of the various scientific devices whose value we have come to appreciate in the past few years. Once more allow us to say that perhaps this entire situation which we have outlined is no problem of the medical profession at all. When one compares the cost of medical care to that spent annually for cosmetics, whisky and automobiles, one often wonders why the family doctor should be concerned about people's problems in regard to their health. They seem to have money for everything else except for their own welfare. We do not know any reason why we should be especially concerned about something which does not seem to interest the average patient himself.

Some method of making it possible for borderline patients to have access to hospital, laboratory and x-ray facilities is pointed to as the real problem in arranging for the care of the low income or so-called borderline patients. The Study Committee looks to the committee of the state medical society which is studying arrangements for hospital insurance for assistance in meeting this problem, as it is believed that prepayment for the use of hospital and diagnostic facilities would not only make it possible for borderline patients to have greater access to such facilities but also that physicians would have a greater likelihood of collecting moderate fees.

The economic plight of the farmer, the industrial worker and the other persons in the low income group colors the whole problem of providing them with medical services. It was pointed out that the Rock County Relief Department has liberalized its views with regard to borderline patients and is now attempting to pay for medical services for certain low income families. However, the need of these individuals has to be great and they are given a thorough investigation before a physician is authorized to care for them. A special arrangement for the care of the low income group was suggested by the Study Committee as follows:

We recommend that some system of reduced fees on a pro rata system be adopted at the next session of our house of delegates. In order that the medical profession may care for the low income groups in an ethical manner, it shall be universal and have the approval of the entire profession.

The committee also reported on the efforts of other organizations to help in the care of the sick in Rock County. The first of these is the Welfare Department, which receives money from the community chest to make loans to borderline patients for medical emergencies. The local clubs of fraternal orders also undertake to give assistance to certain groups of borderline persons. For example, one club arranges each summer to have tonsils removed from children whose parents are unable to care for them. Another club arranges to pay for eye examinations and glasses for certain persons in the county. A philanthropic organization arranges to care for crippled children with funds raised through the sale of crippled children's stamps. There are also several mutual benefit associations which assist employees and sometimes their dependents to receive medical care.

Most of these organizations have the cooperation of the medical society in their endeavor to make it possible for low income persons to receive more medical care. However, some of the arrangements are organized or operated in a manner which interferes with good medical practice and consequently causes dissatisfaction. For example, some fraternal orders to encourage membership have offered members medical service for minor illnesses by contracting with a certain doctor who is willing to provide services for the assessments of 25 cents to 50 cents monthly from each member. Such lodge practice has almost invariably been condemned by medical societies because it provides members with a meager, unsatisfactory service. The organization arranging for the care of crippled children is also criticized because of the tactics it uses to induce physicians to care for crippled children—while claiming credit for all the results achieved. The restrictions of the payment for care of crippled children and the aforementioned regulation whereby patients are sent to the Wisconsin General Hospital are also instanced as undesirable for proper and economical care of crippled children.

In reviewing the general thoughts which have been evolved as a result of the survey, the Study Committee concluded that "the medical profession must make arrangements to take the lead in all things medical" and that:

In general, doctors should be ashamed of themselves to have to admit that certain lay groups can point out the errors of our ways. The medical society should encourage constructive thinking along these lines and urge its members to get busy and keep the control of things medical with the doctor. We hope that the articles which are appearing in the lay press of today in regard to medical practice will soon make doctors conscious of the fact that they must begin to solve many of these public health problems for themselves and not wait until the government forces us to change our entire methods of practice. In other words, we should not be afraid to change our views in regard to the care of the sick but must keep our minds open to suggestion so that the medical profession will retain the position of honor which it has always enjoyed.

GRADUATE MEDICAL EDUCATION: CALIFORNIA

A PROGRESS REPORT OF THE FIELD STUDY ON GRADUATE MEDICAL EDUCATION IN THE UNITED STATES BEING CONDUCTED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

In 1935 the house of delegates of the California Medical Association decided to sponsor a series of statewide graduate courses for physicians in cooperation with the state's four medical schools. The University of California Medical School had been conducting extramural graduate instruction in central and northern California in 1934 and 1935, teams of faculty members participating in extension courses on alternate Fridays and Saturdays during each month of the school year. The data developed from this series were made available to a state association committee appointed to elaborate a program of statewide meetings and clinical conferences. The committee on postgraduate activities consisted of three members, with Dr. Clarence G. Toland chairman and the secretary of the state association as an ex officio member. In February 1937 members of the committee met with the deans of the medical schools, the secretary of the California Tuberculosis and Heart Association and Dr. Charles A. Dukes, chairman of the state association's committee on public relations.

A cooperative and uniform program was adopted, since it was realized by all that postgraduate activities were the most important means of raising the standards of the medical profession. The following proposals were made and put into effect: Medical schools and the state medical association were to cooperate in postgraduate conferences to avoid conflicting programs. Courses were to be arranged through the office of the executive secretary of the state association. At each graduate session an attempt would be made to cover one subject completely with a physician, surgeon, pathologist and roentgenologist participating. Conferences were to include clinical demonstrations. Local physicians with difficult cases were urged to present patients. Expenses incidental to the program were to be borne by the state association and county medical societies. Clinicians who conducted courses were to be reimbursed for travel and hotel expenses. The California Tuberculosis and Heart Association offered to provide half the expense of conferences held in lieu of its meetings. Instructors were to be selected from the medical school faculties and speakers were suggested by the tuberculosis and heart association, by the cancer committee of the state medical association and by other members of the state association. Other medical and health agencies were urged to join in this graduate effort. A five year study program putting these proposals into effect was published in November 1937.[1] Three hundred physicians and other educators offered their services under this plan.

During 1937 conferences were held in seven centers in central and southern California. The graduate committee in each local county society chose subjects from the list supplied by the state association. Of the 103 subjects offered, instruction was sought most frequently in obstetrics, gastro-enterology, pediatrics, gynecology, endocrinology, pharmacology and the clinical use of drugs, traumatic surgery, general surgery, fractures and orthopedics, cardiovascular disease, tumors and allergy. Other courses included symposiums on ear, nose and throat diseases, clinical pathologic conferences, laboratory examinations, dermatology, pneumonia, thyroid and venereal diseases. Nine hundred and fifty physicians registered for graduate training during the first year. The state association expended $441 during 1937 for postgraduate instruction. Each county society selecting a program shared in its support. The estimated cost of postgraduate conferences for the current year is $4,000. The chairman of the present committee on postgraduate work of the California Medical Association is Dr. John C. Ruddock.

One county society, San Joaquin, established in 1935 a permanent annual series of graduate meetings. It was proposed that each year an out of state speaker be invited to participate. At each of the seven evening programs one or more instructors would cover various phases of the subject presented. In 1935 eleven physicians instructed forty-eight members in obstetrics, thyroid, rectal, gastro-enteric and venereal disease, endocrinology and fractures. Each session lasted from two to three hours. A special fee of $5 was charged for the series. This was sufficient to finance travel expenses of guest lecturers, to obtain projection equipment and to supply certificates of attendance to members of the society who were present at least 80 per cent of the time. A record of attendance showed that thirty-eight physicians attended six of the seven meetings.

In 1936 Dr. C. A. Broaddus, first chairman of the San Joaquin county society's committee, obtained, with the aid of the San Francisco Academy of Medicine, an out of state university professor who conducted a clinic on blood diseases. Eleven other lecturers considered such subjects as pediatrics, fractures, abdominal surgery, blood, eye, mouth and throat disease, and chest diseases including roentgenology.

In 1937 the county society's graduate committee of five members organized a series of lectures on syphilis, gonorrhea, pharmacology, obstetrics and gynecology, and traumatic surgery. There is greater interest in graduate work each year, and in 1937 to encourage attendance a $25 prize was offered to the member who wrote the best review of the course.

The annual meetings of the state association are devoted in part to graduate instruction. At the 1938 session three case histories were discussed in clinical pathologic conferences by out of state guest speakers, physicians, surgeons and pathologists. This year an out of state speaker gave a series of illustrated lectures on syphilis at the annual meeting and at twelve county society meetings throughout the state. His expenses were paid in part by the California Department of Public Health. At the annual sessions symposiums, conferences and illustrated lectures characterized the scientific meetings. The attendance in 1938 was 1,970. Of the 11,278 registered physicians in California, 5,906 are members of the state association.

From April 13 to 16, 1938, the University of California Medical School gave a short course of lectures and clinics on diseases of the digestive tract. Twenty-two members of the staff participated. Clinical presentations, outlines of treatment, and demonstrations of diagnostic and therapeutic procedures were designed to meet the needs of practicing physicians. Sessions lasted from 8 a. m. to 9 p. m. on two days and from 8 a. m. to 5 p. m. and 8 a. m. to 12 m. the two remaining days. At the conclusion of each lecture period questions were allowed. There was a two hour round table discussion. Subjects included amebiasis, intestinal worms, diabetes, constipation, intestinal obstruction, tumors and disorders of the stomach and colon, diseases of the rectum and gallbladder, appendicitis, digestive diseases of children, gastro-enteric neuroses and a discussion on vitamins. A tuition fee of $20 included the cost of meals, a mimeographed list of diets referred to in the course and a syllabus. Announcements were sent to alumni practicing in western states and notices appeared in state and national medical journals. Thirty-eight California and five Oregon physicians enrolled.

In August and September 1937 the state university medical school in collaboration with the California Department of Public Health gave a five weeks intramural course on venereal diseases with night lectures twice weekly, members of the faculty participating. Two sessions were devoted to bacteriology and pathology, three to pharmacology, four to practical clinical management and one to public health aspects of the problem. Demonstrations of clinic cases supplemented the lectures. All practicing physicians were invited. No registration fees were charged.

The University of California Hospital and Clinic offers diagnostic facilities to rural physicians of the state who desire consultative services. Patients unable to afford adequate medical examinations may be referred to the university's medical center for study. After a comprehensive investigation, patients are returned to their own physicians with the staff's report and recommendations. This is considered a practical postgraduate conference. Over the past ten years more than 2,200 practicing

1. Supplement to California and Western Medicine **47**: 1-13 (Nov.) 1937.

physicians have availed themselves of this service. From 300 to 360 patients from rural areas are seen in the clinic each month.

The California legislature in 1931 established a state medical library under the control of the University of California to supply registered physicians, surgeons and medical institutions with medical library services, and $42,176 was allocated from the contingent fund of the Board of Medical Examiners for its support. An office was established at the state university medical library in San Francisco, and a southern section was established in Los Angeles. Reference service was offered and the resources of this university's library were made available to physicians of the state. Books, journals, reports, documentary reports or other material were available for loan for seven day periods, subject to transportation charges.

During the first year a librarian visited practicing physicians outside the metropolitan areas of the state, personally interviewing approximately 12 per cent of the profession. A circulating periodical service was established enabling physicians to receive regularly one or more journals in fields of special interest. Books not on reserve were mailed on request. Analysis of items lent to June 1933 showed that 607 borrowers in 140 communities had used 1,049 books and journals. At present approximately 875 physicians are using the facilities of the two sections of the state medical library. Periodicals most frequently desired are those relating to surgery, pediatrics and otorhinolaryngology. Other special journals in laboratory diagnosis and biochemistry also are in demand. British and German specialty journals are extensively circulated. The state medical library cooperates with the Lane Medical Library in San Francisco and the Barlow Medical Library in Los Angeles.

Four years ago, Stanford University School of Medicine offered a series of postgraduate review courses in cooperation with the San Francisco Department of Public Health. The six courses offered during one week in September 1935 were in cardiology, diseases of the chest, obstetrics and gynecology, syphilis, proctology and surgical anatomy for general physicians and a course for specialists in ophthalmology. Instruction was given each morning from 8:30 a. m. to 12 m. in three general courses and from 1:30 to 5 p. m. in three others. A physician could register for one morning and one afternoon course. Three evening lectures were held during the week in nephritis, hypertension, endocrinology and gastro-enteric diseases. More than twenty-eight staff physicians participated in the general instruction and five in the specialty series. Training was available at clinics, demonstrations, examinations of patients in the outpatient department and wards, in pathologic, roentgenologic, medical and surgical symposiums and in a dissecting room. Announcements were sent to all practicing physicians in California and to the secretaries of county medical societies in Oregon, Washington, Nevada, Utah and Arizona and the component societies of Hawaii. Notices appeared in state and national medical and scientific journals. A registration fee of $20 was charged in 1935, when 149 physicians enrolled. Courses in obstetrics, proctology, cardiology and anatomy were popular.

In 1936 there were four morning courses in obstetrics and gynecology, gastro-enterology, pediatrics and cardiology (enrolment limited to fifteen) and four afternoon courses in hypertension and nephritis, neurology and psychiatry, fractures and traumatic surgery and proctology (limited to fifteen physicians). A morning and afternoon course was given in otorhinolaryngology for specialists. General evening meetings on roentgen therapy, backache, blood diseases and syphilis were included. More than fifty members of the faculty instructed 183 physicians who registered. Greatest interest was shown in fractures, traumatic surgery, obstetrics and gynecology, gastro-enterology and hypertension and nephritis.

Eight courses were offered to practicing physicians in 1937. These were on x-ray diagnosis and therapy (for physicians with experience in this field), emergency surgery and fractures, diseases of the genito-urinary tract, cardiology and electrocardiography, diagnosis and treatment of malignant tumors, surgical anatomy and operative technics (additional fee of $10, enrolment limited to twenty-four) and the diagnosis, treatment and control of syphilis. Ward rounds in medicine (limited to fifteen physicians) and clinics in the medical specialties, including clinical pathologic conferences, were provided. A general meeting on the evaluation of new drugs and another on problems in industrial health were held on two evenings. One hundred and thirty-nine physicians registered; two thirds of them had not previously enrolled. Emergency surgery, medical specialties, malignant tumors, cardiology and surgical anatomy were the courses best attended. A comprehensive syllabus with references, charts, diagrams and tables on malignant tumors was supplied to physicians enrolling for instruction in this subject. Registration fees in 1936 and 1937 were $25. The facilities of the medical school and of the San Francisco Hospital were utilized for this graduate training.

Stanford University School of Medicine has, in addition to cooperating in the state association's graduate program, supplied county societies in northern and central California with teams of faculty members on request. Seven sections of the state have been furnished with programs recently.

The medical education committee of the Alumni Association, College of Medical Evangelists, has sponsored a postgraduate assembly in the fall of each year since 1934 and a clinical congress each spring since 1932. The chairman of this committee, Dr. G. M. Taylor, is assisted by four other members. At the postgraduate assembly eighteen lectures are given at half hour intervals during one day from 9 a. m. to 9 p. m., time being allowed for luncheon and dinner. All fields of medicine are considered. Speakers include members of the faculties of the state's three other medical schools and one or more lecturers of international reputation. All practicing physicians are invited and the attendance has varied from 400 to 500 each year.

The clinical congress held in the spring is conducted by members of the faculty of the College of Medical Evangelists. Morning symposiums, afternoon clinics, demonstrations and exhibits and early evening lectures followed by a clinical pathologic conference characterize the day's program. This year symposiums were devoted to the preoperative and postoperative care involved in surgical specialties, including anesthesia and medical complications. Ten physicians and surgeons participated in symposiums. In the seventeen demonstrations and exhibits thirty members of the faculty considered such subjects as fever therapy, orthopedic surgery, proctology and medical and visual education, utilizing patients, models and motion pictures. A registration fee of $1.50 was charged, no fees being required of medical students, interns or residents. The facilities of the college are used for these graduate assemblies.

The Department of Urology, College of Medical Evangelists, offers a course in diagnostic urology, including diagnostic technics, one morning each week. Two physicians can be accommodated. A fee is charged. A volunteer residency is available in urology. This is of from three to twelve months' duration. A short refresher course lasting from one to two months consists of observations of diagnostic and cystoscopic procedures.

The University of Southern California School of Medicine offers graduate courses in surgical anatomy, material and instruction being available for special dissection in otolaryngologic and neurologic anatomy. Graduate courses are scheduled in other preclinical departments and are open to qualified physicians.

The California Department of Public Health has conducted clinics for crippled children since 1927. Fifty or more patients may be seen in one of these clinics by visiting orthopedic surgeons who consult with the local physicians.

The California Tuberculosis Association has visited approximately three fourths of the counties of the state in connection with case finding studies or educational programs. When a clinic is held the interest and cooperation of the local county society is obtained. Local physicians may participate in the examinations and obtain professional training, including instruction in tuberculosis testing and x-ray interpretation. The annual meeting of the tuberculosis association is held over three days prior to the annual session of the state medical association. In the clinical section last year such subjects as pneumothoracic surgery, symposiums on syphilis and x-rays, and diagnostic problems in tuberculosis were included. The attendance varies usually from 300 to 500.

The Heart Committee of the San Francisco County Medical Society and the San Francisco Tuberculosis Association was organized in 1930. The postgraduate course offered that year

without fee to physicians practicing in northern California was attended by 227 physicians from sixty-five cities and towns. Each succeeding year a two day postgraduate course has been offered with constant increase in interest and attendance.

In 1935 the California Heart Association was organized and expanded the postgraduate activities initiated by the San Francisco committee. The eighth annual postgraduate symposium was held in November 1937. The facilities of ten local hospitals were used with lectures, demonstrations, afternoon study groups —each limited to from five to ten physicians—and case presentations. Members of the faculties of the two medical schools in San Francisco and other physicians conducted the symposium. A fee of $2 was charged for two days' training. Three hundred practicing physicians registered and a mimeographed syllabus was supplied to each.

The Los Angeles Heart Association offers an annual course for physicians practicing in the southern part of the state. A round table discussion of the physiologic, clinical and pathologic problems in heart disease featured the 1937 fifth annual symposium. In addition to lectures, exhibits of pathologic specimens and electrocardiograms were on display at the Los Angeles County Medical Association Building. A $2 fee was charged.

In 1938 the California Heart Association held a four day symposium concurrently with the annual meeting of the California Medical Association. This was arranged by the state medical association's committee on postgraduate work.

OFFICIAL NOTES

DATE OF ST. LOUIS SESSION

The next annual session of the American Medical Association will be held in St. Louis, May 15 to 19, 1939.

THE RADIO PROGRAM "YOUR HEALTH"

Resumption of Broadcasts October 19 for Thirty-Six Weeks

The American Medical Association and the National Broadcasting Company will resume the radio program Your Health beginning Wednesday October 19 and running consecutively for thirty-six weeks thereafter. The program will be broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. Eastern Standard time (1 p. m. Central Standard time, 12 noon mountain time, 11 a. m. Pacific time).

This will be the fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health. The radio scripts will be written by Leslie Edgley, an independent radio script writer affiliated with the Artists' Bureau of the National Broadcasting Company and author of the successful radio dramatic feature "There Was A Woman." Material for the scripts will be furnished by the Bureau of Health Education of the American Medical Association.

The medical societies can do much to influence the local radio stations to carry this program, by showing an interest in it and by informing the local manager, as well as the local school authorities.

The following is a list of the stations connected with the Blue network of the National Broadcasting Company, but no assurance can be given as to how many of these stations will broadcast the program Your Health:

Basic Blue Network

WJZ	New York	WEBR	Buffalo	KSO	Des Moines
WBZ	Boston	KDKA	Pittsburgh	KOIL	Omaha
WBZA	Springfield	WHK	Cleveland	WREN	Kansas City
WEAN	Providence	WSPD	Toledo	WLW	Cincinnati
WICC	Bridgeport	WXYZ	Detroit	WCKY	Cincinnati
WFIL	Philadelphia	WOWO	Fort Wayne	WSAI	Cincinnati
WBAL	Baltimore	WENR-WLS	Chicago	WRTD	Richmond
WMAL	Washington	KWK	St. Louis	WABY	Albany
WSYR	Syracuse	WMT	Cedar Rapids	WJTN	Jamestown,N.Y.
WHAM	Rochester	WTCN	Minneapolis-St. Paul	WLEU	Erie

Supplementary Facilities

WFEA	Manchester, N.H.	WFBC	Greenville	KVOD	Denver
WBRE	Wilkes-Barre	WWNC	Asheville	KLO	Ogden
WSAN	Allentown, Pa.	WIS	Columbia	KIDO	Boise
WORK	York, Pa.	WCSC	Charleston	KGIR	Butte
WCOL	Columbus, O.	WJAX	Jacksonville	KPFA	Helena
WGL-WOWO	Ft.Wayne	WFLA-WSUN	Tampa	KGHL	Billings
WOOD	Grand Rapids	WIOD	Miami	KSEI	Pocatello, Ida.
WBOW	Terre Haute	WMC	Memphis	KTFI	Twin Falls, Ida.
WGBF	Evansville	WSB	Atlanta	KGO	San Francisco
WEBC	Duluth-Sup'rl'r	WBRC	Birmingham	KECA	Los Angeles
KSOO-KELO	Sioux Falls, S.D.	WJDX	Jackson	KEX	Portland, Ore.
KANS	Wichita	WSMB	New Orleans	KJR	Seattle
WTAR	Norfolk	WALA	Mobile	KGA	Spokane
WPTF	Raleigh	WROL	Knoxville	KFBK	Sacramento
WSOC	Charlotte	WAVE	Louisville	KWG	Stockton
		WSM	Nashville	KMJ	Fresno
		WTMJ	Milwaukee	KERN	Bakersfield
		WIBA	Madison		

The programs to be broadcast in the first group, together with their dates and their topics, are as follows:

October 19, What is Health?
October 26, Growing Strong.
November 2, Seeing and Hearing Well.
November 9, Healthier Boys and Girls.

These programs will be broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

MEDICAL ECONOMIC ABSTRACTS

STATE MEDICINE PROPOSED IN NEW ZEALAND

In spite of its international fame for morbidity and mortality rates lower than those of any country with sickness insurance or state medicine, the Labor Party, now in power in New Zealand, has presented a program of social pensions which includes "a universal general practitioner service free to all members of the community who require medical attention."[1] The Prime Minister states that the scheme embraces free hospital or sanatorium treatment for all, free medicines and free maternity care, including maintenance in a maternity house and a grant to assist mothers in special circumstances to provide outfits for their babies. No provision is made for specialist services outside of hospitals, although some statements from the government indicate an intention to add these later. Critics charge that the additional expenses required by the additional and increased pensions plus the medical service will almost double a present very high tax rate.

Some form of sickness insurance has been under discussion for several years. Representatives of the New Zealand Branch of the British Medical Association have held numerous conferences with members of the ministry to discuss proposed medical programs and, while agreeing to do their best with whatever scheme might be introduced, have insisted that since the results achieved in the protection of health under the system of private practice in New Zealand were already so greatly superior to those obtained in countries with sickness insurance and state medicine, it would be better to develop and improve that system than to abandon it in favor of any universal governmental scheme of medical practice.

Just how closely the medical professions agree on the effect of contract and governmental schemes of medical care on the

1. (*a*) New Zealand Herald, April 4, 1938; (*b*) National Health Insurance Section, Supp., New Zealand M. J. **37**: 9 (April) 1938.

quality of the medical service is illustrated by the following extracts from a statement of the chairman of the National Health Insurance Committee of the New Zealand Branch of the British Medical Association submitted to the Minister of Health of New Zealand: [2]

The relationship which is established immediately a patient summons a doctor has been, and always will be, a strictly personal relation of a very special sort—independent of fee or the standing of the patient. Medical service has a personal and confidential character which is as many sided as human nature itself and touches at every point in people's lives. The confidence of the patient implies corresponding responsibility on the part of the doctor, and no limits can be set to what may be required of it.

Consequently medical service does not lend itself readily to terms of contract like the supply of a definite number of standard articles, or the giving of so many hours of specified work. Contract necessitates limitation of responsibility. There would be the tendency for the doctor's services to be limited by the terms of the contract rather than by the exigencies of the case. If only part of the doctor's services are on a contract basis, the stimulus of private practice tends to maintain the standard of his contract work.

For this reason contract practice has been and should remain, restricted to conditions in which no other more satisfactory arrangement can be made. . . .

Nowhere does Health Insurance set standards, nor are its standards maintained by its own regulations and definitions. It is unheard of for any one to seek to advance his professional standard and method by study or emulation of Health Insurance work. The standard is set by the best of voluntary, uncontrolled, private or honorary practice, which it is therefore important to preserve in as large a body as possible. . . .

Professional organizations such as the Faculties of Medicine of Universities, the Colleges of Surgeons and Physicians and Medical Associations, such as our own, are the chief agencies through which medical knowledge, system and ideals have been promoted, developed and promulgated. . . . This policy has been responsible for the preeminence of British medicine as similar policy was for the initiative displayed by German medicine two generations ago, and it is for the prestige of American Medicine today. . . .

The adoption of a universal scheme would lead to those very distinctions which it is the object of this association no less than of the government to avoid. A certain number of doctors would prefer to remain outside the scheme, and a certain number of people would prefer to make their own arrangements as they have done heretofore, although being entitled to medical benefits under the scheme. While there might be few who would do this habitually, many would on occasions. Thus there would grow up two types of practice from which we so far, fortunately, have been free—panel practice and private practice. Even if both were in fact equally efficient, the former would come to be regarded as the "poor man's" practice. . . .

Unfortunately the average patient is not conscious of the necessity for treatment to be based on accurate diagnosis, as witness the millions spent on patent medicines. All he asks for is treatment, and under a panel scheme without ancillary services treatment may well become empirical. . . .

What we have all along wished to emphasize is that the promotion of health is a greater object than the treatment of sickness, though we do not underestimate the latter; and that National Health Insurance, being really a system of indemnification for sickness, does not materially advance the greater object.

The medical association suggests, as an alternative to sickness insurance or state medicine, continuation and expansion of the program of health care that has already produced such famous results in New Zealand. It proposes a number of improvements in evironmental conditions, including housing and better working conditions. It points out that "there are admittedly problems of nutrition requiring investigation" and suggests that if these conditions can be improved it "will do more for the people than all the dietary systems in vogue or the entire National Health Insurance formulary of medicaments." The association also urges an extension of preventive and antepartum care and emphasizes, especially, the possibilities open to the extension of research.

In regard to matters of administration the view we take is that National Health Insurance is a system invented over fifty years ago to meet difficulties in other countries which, to a large extent, have been overcome in New Zealand by following lines and methods of our own. The health insurance system involves a complicated administration of its own; and, if we superimpose on our own health administration this borrowed system, a cumbrous structure will result. We consider that it would be wiser before introducing National Health Insurance to review and amend the existing administrative machinery which has developed in an irregular manner during the rapid changes of a century's growth and settlement.

The association urges the extention of health department activity and a reorganization of hospital administration so as to obtain a better distribution both of hospitals and of the service which they supply.

2. Footnote 1*b*, pp. 8-18.

BRITISH NURSING PROBLEMS

Some of the features in "Evidence submitted by the British Medical Association to the Interdepartmental Committee on Nursing Services" [1] suggest interesting comparisons with similar problems in the United States.

"There is, undoubtedly," says the statement, "an insufficiency of candidates of any type for the nursing profession, and the shortage will become still more acute in the near future on account of the extension of hospital accommodation, of the increasing complexity of medical and surgical procedures, and of the reduction of the nurse's hours of work." This shortage is charged to the interruption between graduation from what would be called high school in this country and the opportunity to enter nursing training, and on the strenuousness of the training and the work that accompanies it, as well as the discipline to which the prospective nurse is subjected. Even after graduation the salary and conditions of work suffer by comparison with other occupations.

It is rather surprising to note that it is proposed to meet these conditions by a lowering of professional standards. Military terms seem to have invaded all vocabularies, so that the question of securing additional candidates is treated under the head of "Recruitment." It is urged that discipline be relaxed and opportunities for leisure during the training be expanded.

The discussion of "Terms and Conditions of Service" arouse memories of proposals under the Wages and Hours Bill, although it is recommended that "There should be a maximum working period of ninety-six hours a fortnight," and "one free day in each week." The discussion continues with the statement that "It is desirable that there should be provided within each hospital machinery for the discussion between the hospital authority and the nursing staff of the various problems of mutual interest, including the grievances of nurses."

"Assistant nurses" with lower professional standards are proposed to undertake certain types of nursing. The examinations now given are criticized as too technical, and a "Group System for Training" is proposed by which an association of hospitals in an "appropriate area" would be "linked together to form a *training unit*." It is held that such a system "would probably be advantageous not only to the probationer but to the smaller and special hospitals, which would enjoy the services of a steady stream of partially trained nurses." This proposal sounds much as if the medical profession were to say to the public "We know you should have good medical care at all times, but for the little things that come up we are going to send out a sort of half-trained office girl."

UNITED STATES NOT SO BAD

That the United States is still out ahead of Great Britain in health care seems to be the opinion of Dr. J. O. Dean in a review of the Report on the British Health Services by PEP in the *American Journal of Public Health* (**28**:786 [June] 1938). After an analysis of the material in that comprehensive report, Dr. Dean says:

"PEP will dispel any doubt in the minds of those who feel that conditions of general well-being in the United States are unfavorable in comparison with those of Great Britain. Apparently the British attitude is to 'hit upon' rather than to develop measures fostering health. The reviewer cannot escape the feeling that despite Great Britain's more comprehensive statutory provisions for the relief or prevention of ill health, she lags far behind the United States, largely because there has been lacking a dynamic attitude permitting necessary changes to be effected in the social machinery for the better adjustment of forces producing health."

1. Nursing Problems—Evidence submitted by the British Medical Association to the Interdepartmental Committee on Nursing Services, Supp. Brit. M. J. **1**: 301 (May 14) 1938.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—The Marion County Medical Society will be host to the Northwestern Division of the state medical association at a meeting in Winfield, September 15. The speakers will include Drs. Arthur Neal Owens, New Orleans, "Repair of Facial Defects"; William E. Prescott Jr., Birmingham, "Clinical Use of Ovarian and Pituitary Hormone"; Julius E. Linn, Birmingham, "Anorectal Pain and Its Clinical Significance"; Clayborne R. Whitman, Tuscumbia, "Why Some Bad Results in Obstetrical Practice?" and Ellis Dice Lineberry, Birmingham, "The Anemias, Their Diagnosis and Treatment."

Illegal Practitioner Serves Jail Sentence.—A self-styled "herb doctor," Mrs. A. L. Hinkley, was sentenced July 29 to pay a fine of $500 and costs or to serve 140 days in jail with an additional three months in jail for practicing medicine without a license, newspapers reported. The woman was arrested following several complaints from Negro residents of Mobile that she had defrauded them of money and personal belongings under the pretense that she would cure their afflictions and ills. Two blind witnesses related her promises to restore their eyesight. The defendant denied the allegations but admitted selling the complainants herbs and roots from which they were to make a "tea" for their "stomach trouble." Unable to pay the fine, the defendant went to jail, it was stated.

CALIFORNIA

Plague Infection.—According to *Public Health Reports,* plague infection was recently proved in a pool of fifteen fleas from thirteen chipmunks shot at the Osito Girls' Camp, three miles southwest of Pine Knot, San Bernardino County.

Graduate Courses.—A series of graduate courses will be given at San Francisco Hospital September 12-16 under the auspices of the hospital, Stanford University School of Medicine and the San Francisco Department of Public Health. According to the program, subjects covered in the morning and afternoon will include traumatic injuries, acute abdominal emergencies and fractures, gynecology, diseases of the chest, practical management of hypertension and nephritis in the doctor's office, pediatrics, proctology, and surgical anatomy and operative technic. Courses for specialists in the mornings will be given in anesthesiology and otorhinolaryngology. Speakers at the general meetings in the evenings will be: Drs. David A. Wood, "Surgical Pathology"; Ludwig A. Emge, "Relation of Sex Hormones to Cancer"; Emile F. Holman and Dwight L. Wilbur, "Disease of the Thyroid Gland," and Harry E. Alderson and Merlin T. R. Maynard, "Diagnosis and Modern Treatment of Common Dermatoses."

COLORADO

Denver Creates Medical Service Bureau — Accepts Hospital Plan.—At a meeting of the Medical Society of the City and County of Denver August 16, a resolution was unanimously adopted creating a central service bureau to meet the demand for prepayment care. Dr. Paul J. Connor, Denver, was appointed chairman of a committee to work out the details of the project. At the same time the society approved the plans of the recently incorporated Colorado Hospital Service Association and accepted, without a dissenting vote, the report of its special committee which had negotiated with the service association. The decision to develop a plan for medical care of low income groups followed a survey by the society to determine whether there was a need or demand for any new form of medical practice for low income families among employed groups in the Denver metropolitan area. In the spring of 1938 questionnaires were sent to all employers in the area who employed ten persons or more. Statistical information was obtained regarding the number of employed persons in various groups whose incomes were under $1,200 a year, from $1,200 to $1,500, from $1,500 to $2,000 and so on. Employers were also asked to indicate interest or lack of interest in such plans. Of the 35 per cent who returned full replies, the majority expressed interest in and asked for information concerning a prepayment plan and favored adherence to the basic principles of the American Medical Association. While actual details have not yet been worked out, the plan will be under control of the county society, will guarantee free choice of physician and will abide by the ten principles of the American Medical Association. It will not include hospital service. Cooperative and independent studies by the medical society and the Denver Hospital Council preceded the incorporation of the hospital service association. Mr. William McNary, formerly business manager of the Colorado General Hospital, Denver, was appointed executive director of the association, effective September 1.

CONNECTICUT

Personal.—Lorande Loss Woodruff, Ph.D., professor of protozoology, Yale University School of Medicine, New Haven, has been appointed chairman of the department of zoology and director of the Osborn Zoological Laboratory.

Vacancies for Physicians.—The newly created personnel department of the state of Connecticut announces examinations for positions as assistant sanatorium physician at Undercliff Sanatorium; assistant hospital physician at state mental hospitals; chief physician of crippled children division, bureau of child hygiene, and public health physician, bureau of venereal diseases. Residence in Connecticut is not a requisite. Applications will not be considered unless they are on file in the personnel department, State Capitol, Hartford, September 10 or bear a postmark not later than that date. A separate application should be filed for each position. Application forms may be obtained from the personnel division or at any office of the Connecticut State Employment Service. Candidates must be eligible for a license to practice medicine and surgery in Connecticut and must have had at least one year of general hospital internship in a hospital approved by the American Medical Association. Preference will be given to candidates who have had training or other experience in the care of tuberculous patients and to those with special training in other branches of medicine or surgery.

DISTRICT OF COLUMBIA

Alumni Extension Course. — The third annual alumni extension course of the Georgetown University School of Medicine will be held September 12-16. Out of town speakers will include Drs. Frank H. Lahey, Boston; Dean Lewis, Nicholson J. Eastman and Edward H. Richardson, Baltimore; Jerome Selinger, New York; John Mark Higgins, Sayre, Pa., and Francis C. McCormack, Englewood, N. J. The program has been designed to interest the general practitioner, while a variety of special clinics and conferences have been arranged for specialists. The "silver jubilee class of 1913" is sponsoring the course this year.

GEORGIA

District Meetings.—The Eighth District Medical Society was recently addressed in Waycross, among others, by Drs. Raymond L. Johnson, Waycross, on "Malignancies of Sigmoid and Rectum"; Arthur G. Fort and Lester A. Brown, Atlanta, "Radical Mastoid Operation with Skin Graft" (motion picture); Henry W. Clements, Adel, prevention and treatment of eclampsia, and Henry J. Goodwin Jr., Douglas, ovarian hyperfunction. ——At a recent meeting of the Sixth District Medical Society in Sandersville the speakers included Drs. Paul S. Kemp, Macon, on "Care of the Senile Diabetic"; Charles J. Woods, Macon, "Treatment of Skin Cancer"; Frederick B. Rawlings, Sandersville, "Some Surgical Aspects of Gallbladder Disease"; Robert B. Greenblatt and Everett S. Sanderson, Augusta, "Newer Venereal Diseases"; Robert C. Goolsby Jr., Macon, "Asphyxia Neonatorum"; David Henry Poer, Atlanta, "Differentiation and Treatment of Goiter," and John A. Bell Jr., Dublin, "Pneumococcus Meningitis."——The First District Medical Society was addressed in Savannah July 20, among others, by Drs. George H. Lang, Savannah, "Endoscopic Removal of Foreign Bodies from the Air and Food Passages"; H. F. Sharpley Jr., Savannah, "Practical Application of the Endocrines in the Correction of Abnormal Menstruation"; Shelton Elliott Wilson, Savannah, "Use of Sulfanilamide in Urology," and Robert Drane, Savannah, "Intestinal Obstruction."

ILLINOIS

Personal.—Dr. Loren L. Collins, Chicago, has been appointed full time medical director of the La Salle County Tuberculosis Sanatorium, Ottawa, effective September 1; Dr. Albert J. Roberts has held the position since it was created in 1919 on a part time basis.——Dr. Joseph H. Kinnaman, Charleston, W. Va., has been appointed assistant health commissioner of Peoria with supervision of school health activities, effective

August 15. Dr. Kinnaman formerly served as health officer of Topeka, Kan., as assistant health commissioner of Cincinnati, as instructor, department of pharmacology and materia medica, State University of Iowa College of Medicine, Iowa City, 1927-1930, and as deputy commissioner to the Iowa State Department of Health in charge of child health and health education activities.

Chicago

The National Health Program and American Medicine.—The North Side Branch of the Chicago Medical Society will devote its meeting September 15 to a consideration of "The National Health Program and American Medicine." The speakers will include:

Dr. Olin West, Secretary and General Manager, American Medical Association, The Conference.
Dr. Roger I. Lee, Boston, Trustee of the Association, Teaching and Practicing Medicine.
Dr. William F. Braasch, Rochester, Minn., Chairman, Advisory Committee on Supply of Medical Care of the Association, Progress of the A. M. A. Survey.
Dr. Irvin Abell, Louisville, Ky., President of the Association, American Medicine.
Dr. Morris Fishbein, Editor of THE JOURNAL, will open the discussion.

A dinner will precede the meeting, which will be held at the Drake Hotel. The meeting is open, but dinner reservations should be arranged through Miss Wolf, Randolph 0244.

Business Joins Campaign Against Syphilis.—A drive against syphilis will be launched in the city, September 5, by business groups, who will participate in a campaign started last year by the Chicago Department of Health under the auspices of the U. S. Public Health Service. Included in the cooperating agencies are the State Street Council, representing major loop merchants; the Chicago Association of Commerce, representing leading industries; the Cook County Retail Council, an organization of community merchants, and the Illinois Federation of Retail Associations, representing twenty-one city and state merchant associations. Their first step will be to provide educational and lecture material on syphilis for all employees, according to the Chicago *Tribune*. It was stated that thirty-three concerns, including steel companies, drug stores, laundries, restaurants and bakers, have provided syphilis testing programs for their employees since last April. Since last November, when the field tests began, 79,533 have volunteered, including 7,421 high school and college students and 6,742 grade school pupils.

INDIANA

Personal.—Dr. George W. Kohlstaedt was elected president of the Indianapolis board of health August 4, succeeding Dr. Maurice Joseph Barry, who has served since 1932. Frank G. Laird was elected vice president, succeeding Dr. Leonard A. Ensminger. Dr. Herman G. Morgan began his twenty-sixth year as secretary of the board August 12.

Changes in Health Department.—Dr. Lewis C. Robbins has been appointed acting chief of the bureau of local health administration of the state department of health during the absence of Dr. John W. Ferree, chief of the bureau. Dr. Ferree was to begin a year's graduate work at Johns Hopkins University September 1. Dr. Albert W. Ratcliffe has been appointed assistant to Dr. Clyde G. Culbertson, chief of the bureau of bacteriology and pathology. He graduated at the Indiana University School of Medicine, Indianapolis, in 1936.

IOWA

Spotted Fever.—A case of Rocky Mountain spotted fever was reported to the state department of health, July 13, by Dr. Ross E. Gunn, Boone, in Boone County. June 23 the state hygienic laboratory reported a positive Weil-Felix agglutination reaction on a serum specimen sent to the laboratory by Dr. Robert E. Dwyer, Preston, in Jackson County.

KANSAS

Committee on Automobile Accidents.—The Kansas Medical Society has appointed a committee on automobile accidents with the following members: Drs. Arthur K. Owen, chairman; John L. Lattimore, Harold W. Powers and Fred P. Helm, all of Topeka.

Personal.—Dr. Henry A. Dykes, Wichita, has retired as chief medical officer of the Veterans Administration Facility in Wichita after holding the position seventeen years; he will be succeeded by Dr. George E. Tooley.——Drs. Ova P. Davis and William L. Warriner, Topeka, were guests of honor at a banquet given by the Shawnee County Medical Society in Topeka recently in recognition of their completion of forty years in the practice of medicine.——Dr. Roy B. Weathered, Kansas City, Mo., will succeed Dr. Lawrence F. Steffen, El Dorado, as health officer of Butler County.——Dr. Samuel M. Hibbard has been elected mayor of Sabetha.

MASSACHUSETTS

Society News.—Dr. George W. Morse, Boston, was recently elected president of the Massachusetts Society of Examining Physicians and Dr. Matthew Norton vice president. Drs. Robert C. Gwin and William Pearce Coues, Brookline, were reelected treasurer and secretary respectively.

Personal.—Dr. Elliott P. Joslin, Boston, will deliver the two Malthe lectures and conduct a clinic in Oslo, Norway, September 5-7; he will also participate in a symposium on protamine insulin with Dr. H. C. Hagedorn, Copenhagen, and Dr. Wilhelm Falta, Vienna, before the Gesellschaft für Verdauungs- und Stoffwechsel-Krankheiten in Stuttgart September 23.

Resolution Opposes Exclusion of Nonmedical Workers as Health Officers.—At a meeting of the Massachusetts Public Health Association June 30 a resolution was adopted recording its opposition to the report of the National Health Officers Qualifying Board to the United States Conference of Mayors so far as it excludes properly trained and otherwise qualified nonmedical public health workers from serving as health officers. The resolution points out that public health work is not limited exclusively to medical subjects and knowledge but is inextricably dependent on engineering, bacteriology, chemistry, physics, sanitation, vital statistics, nutrition, public health education and other highly scientific but nonmedical pursuits. The resolution is based on the report published in the *American Journal of Public Health*, January 1938, recommending that only physicians shall be eligible to serve as health officers in American cities.

MICHIGAN

Change in Speakers at State Meeting.—Dr. William S. Sadler, Chicago, will address the county secretaries' conference September 20 during the annual meeting of the Michigan State Medical Society in Detroit. His subject will be "The Grand Opportunity for Leadership by the County Medical Society." Dr. Harrison H. Shoulders, Nashville, Tenn., speaker of the House of Delegates of the American Medical Association, who was originally scheduled to address the conference, is unable to attend.

Graduate Course in Internal Medicine.—Wayne University College of Medicine and Receiving Hospital, Detroit, will offer a graduate course in internal medicine September 12-17. Two hours daily will be devoted to bedside diagnosis and treatment. Ward rounds will be conducted with groups of from four to six persons so that each physician will have the opportunity to examine every patient. Lectures on recent advances in therapeutics will also be included. Any licensed physician may enroll in the course.

Personal.—Dr. Russell E. Pleune, Lansing, formerly in charge of the bureau of venereal disease control for the state department of public health, has been named director of the Dickinson County health unit, effective September 1; he succeeds Dr. Clifton E. Merritt.——Dr. Christopher J. Stringer, Detroit, has been appointed superintendent and medical director of the Ingham Tuberculosis Sanatorium, Lansing, succeeding Dr. George C. Stucky, who had held the position since 1925. Dr. Stucky has been appointed director of the Eaton County Health Department, effective September 1; he fills the vacancy left when Dr. Thomas E. Gibson, Paw Paw, resigned to accept a similar position in Van Buren County.——Dr. Fred R. Hanna has been appointed superintendent of the State Home for the Feebleminded at Lapeer; he has been acting superintendent at the institution since May 1937.

MINNESOTA

Chiropractor Jailed—Abortions.—Herman V. Feenstra, 65, an itinerant unlicensed chiropractor, was sentenced by Judge Joseph Moriarty, Shakopee, August 10, to a four year term in prison, according to the state board of medical examiners. Following his arrest August 8 Feenstra pleaded guilty to a charge of performing illegal operations. According to the board, Feenstra stated he was born at Ackley, Iowa, and that he graduated from the Davenport School of Chiropractic in 1922. He located at Elkton, S. D., but lost his license when he became involved in illegal practices. He was convicted in South Dakota on an abortion charge and was arrested for

manslaughter, drunken driving and rape. The clerk in Brookings stated that Feenstra jumped a $2,500 cash bond January 19 in the rape case. When apprehended, Feenstra had two grips in his car containing instruments for performing abortions. His records indicate that he has performed hundreds of these operations, charging from $15 to $300 per patient, the board stated.

MISSISSIPPI

Health Officers' Conference.—A meeting of county health officers was scheduled to be held in Jackson August 8-9. The theme of the session was the control of syphilis, and the speakers included Drs. Felix J. Underwood, state health director; Archie L. Gray, state director of communicable disease control; Dolph V. Galloway, Meridian; Henry V. Ricks, John A. Milne, Jackson; Alton R. Perry, Laurel; Andrew Hedmeg, Natchez; Martin T. Van Studdiford, New Orleans; Charles R. Gillespie, Indianapolis; Robert H. Dejarnette, Rolling Fork, and W. E. Noblin, Jackson.

NEW JERSEY

Conference for County Society Officers.—The Medical Society of New Jersey has invited officers of county medical societies to meet in Trenton September 11 for a "training conference." Following a luncheon there will be first a combined conference of all officers and later separate conferences, one for presidents and vice presidents and another for secretaries, historians and reporters. Among the subjects to be included will be county society committees, county society membership, survey of medical needs and supplies, the art of presiding, county society bulletins and activities of the state society.

Institute for Medical Research.—The Squibb Institute for Medical Research "to create in the medical and biological fields an industry-supported research enterprise" has been organized by E. R. Squibb and Sons at New Brunswick with a new laboratory building recently completed at a cost of $750,000. Dr. George A. Harrop, formerly associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore, will be director of research in direct charge of the institute and in addition will head the division of experimental medicine. There will be three other main divisions and in addition there will be a biochemical laboratory and a medicinal chemistry laboratory. Dr. Harry B. Van Dyke, professor of pharmacology, Peiping Union Medical College, Peiping, China, will be head of the division of pharmacology; Dr. Geoffrey W. Rake, former research associate in the Connaught Laboratories, University of Toronto, the division of bacteriology and virus diseases, and Erhard Fernholz, formerly of Princeton University, the division of organic chemistry. Hans Jensen, Ph.D., formerly of the laboratory of endocrine research, Johns Hopkins University, Baltimore, will be in charge of the biochemical laboratory, and William A. Lott, M.S., who has been head of Squibb's research group since 1926, in charge of the laboratory of medicinal chemistry. Other appointments are as follows:

Roy O. Greep, Ph.D., formerly instructor at Harvard University, Cambridge, Mass., and Bacon F. Chow, Ph.D., associate professor of biochemistry, Peiping Union Medical College, Peiping, China, to the division of pharmacology.

Arthur E. O. Menzel, Ph.D., instructor in biologic chemistry, Columbia University, New York, and Morris F. Shaffer, Ph.D., assistant in bacteriology, Harvard, to the division of bacteriology and virus diseases.

Homer E. Stavely, Ph.D., formerly research fellow in chemistry, Yale University, New Haven, Conn., and Harold B. MacPhillamy, a graduate student in the department of organic chemistry, Columbia University, New York, to the division of organic chemistry.

Sybille Tolksdorf, recently engaged in research at the Institute of Experimental Biology, University of California, associate in the biochemical laboratory.

Frank H. Bergeim and David F. Menard, Ph.D., members of the Squibb staff, associate and assistant respectively in the laboratory of medicinal chemistry.

Stefan Ansbacher, D.Sc., of the Squibb staff since 1937, associate in the division of experimental medicine.

The division of experimental medicine is working out a plan of hospital affiliation to provide clinical facilities. A ward of fifteen or twenty beds will be maintained for the observation of patients in connection with research problems at the institute. Under the direction of this division, new fellowships in medical schools will be established and existing fellowships will be continued as part of the institute's program. Dr. Harrop, a native of Illinois, graduated in 1916 from Johns Hopkins' medical school and was a member of the faculty from 1924 to 1937. The new laboratory building will be dedicated early in October.

NEW YORK

Conference on Problems of Rural Medicine.—A conference on the problems of rural medicine sponsored by the staff of the Mary Imogene Bassett Hospital, Cooperstown, will meet October 7-8. The subjects to be considered are rural morbidity and public health programs in rural areas; postgraduate medical education in rural areas and the economics of rural medicine, including the rural hospital, the rural physician and the member of a rural community. The advisory committee for the conference consists of Drs. Marion A. Blankenhorn, Cincinnati; Frank G. Boudreau, executive director, the Milbank Fund, New York; Thomas P. Farmer, Syracuse, chairman of the council committee on graduate education, Medical Society of the State of New York; Edward S. Godfrey Jr., state health commissioner, Albany; Harry S. Mustard, professor of preventive medicine, New York; Willard C. Rappleye, dean, College of Physicians and Surgeons, Columbia University, New York; Ray Lyman Wilbur, president of Stanford University; Mr. Dan D. Casement, Juniata Farm, Manhattan, Kan.; Michael M. Davis, Ph.D., chairman, committee on research in medical economics, New York; Louis I. Dublin, Ph.D., third vice president, Metropolitan Life Insurance Company, New York; Lowell J. Reed, Ph.D., dean, Johns Hopkins University School of Hygiene and Public Health, Baltimore, and Mr. Owen D. Young, chairman of the board of the General Electric Company, New York.

New York City

Hospital News.—A new x-ray department was recently dedicated at Long Island College Hospital, Brooklyn, with Dr. Francis Carter Wood as the principal speaker at the ceremony. The new department, which cost $67,000, includes a 400,000 volt roentgen therapy machine and is under the direction of Dr. Alfred L. L. Bell. It is named in honor of the late Albert L. Mason, a former president of the hospital.

Psychologic Clinic for Policemen.—The Patrolmen's Benevolent Association has established a psychologic clinic for policemen in difficulties, with a policeman-psychologist in charge. The New York *Times* reports that the clinic is an effort to prevent suicide among the men because of personal troubles. The principal causes of suicide listed are carrying life insurance beyond income allowance, buying furniture and other possessions on credit, helping needy relatives, acting as endorser for friends and relatives who fail to repay loans, gambling in the hope of paying off debts, buying too expensive a home, running up large medical bills instead of first seeking the advice of the police surgeon, entertaining beyond means, and keeping children in private schools. Plans have been made for the assistance of psychiatrists in psychiatric cases.

WPA Workers Withdrawn from Hospitals.—Assignments of 3,289 WPA workers in the twenty-six city hospitals were to be ended August 27 on an order from Washington closing the hospital project, the New York *Times* reported August 18. The order stated that employment of relief workers in jobs that should be included in the city budget could no longer be sanctioned. During the five years since the first relief workers were brought into the department their duties have come to overlap many of those of the regular employees, according to Dr. Sigismund S. Goldwater, hospital commissioner; he estimated that replacements would have to be found for at least 35 per cent of them, although the condition of city finances gave little hope of additional funds. According to WPA officials, the project saved the department of hospitals about a million dollars a year.

NORTH CAROLINA

Deaths from Tetanus Increase.—Seven deaths from tetanus occurred in North Carolina during July, bringing the total of deaths for the year to twenty-three as compared with twenty-one for the entire year 1937 and twenty-nine for 1936.

Society News.—The Buncombe County Medical Society was addressed August 1 by Dr. Karl Schaffle, Asheville, on "The Value of Inspection in Physical Diagnosis."——Dr. Lewis W. Elias, Asheville, recently addressed the Catawba Valley Medical Society on "Colitis in Children."

Personal—Dr. Joseph Lindsay Cook, Winston-Salem, assistant county health officer and medical superintendent in charge of the Forsyth County Hospital, has resigned to take charge of a syphilis control program in Guilford County.——Dr. Henderson Irwin, Eureka, was honored with a supper by citizens of the community recently on his fifty-second birthday. Six hundred persons attended. He has been in Eureka twenty-five years.

Beauty Shop Workers Required to Have Wassermann Tests.—The North Carolina state board of cosmetic arts examiners has announced that all new applicants for licenses to work as "beauticians" who file for the next examination in October must present certificates showing that they have had Wassermann tests. In addition, the certificate will be required of all workers who henceforth apply for renewal of licenses. When such tests are positive, the examining board may require treatment before issuing the licenses. This action was taken following a conference with the state board of health, which is working out an extensive program for the control of venereal disease.

NORTH DAKOTA

Dr. Skelsey Secretary of State Society.—Dr. Albert W. Skelsey, Fargo, was reelected secretary of the North Dakota State Medical Association at the recent meeting. Dr. William W. Wood, Jamestown, is treasurer and not secretary, as stated in a news item in THE JOURNAL, August 20, page 728.

OHIO

Society News.—Dr. Harold H. Wagner, Dayton, addressed the Greene County Medical Society in July on "Vaginal Discharge: Its Diagnosis and Treatment."——Dr. John H. Skavlem, Cincinnati, addressed the Hempstead Academy of Medicine June 13 in Portsmouth on "Tuberculous and Nontuberculous Chronic Lung Infections."

Promotions at Cleveland. — Among promotions on the faculty of Western Reserve University School of Medicine, Cleveland, recently announced were the following:

Dr. Harold Feil, associate clinical professor of medicine.
Dr. Donald M. Glover, associate clinical professor of surgery.
Dr. Robert L. Faulkner, assistant professor of gynecology.
Dr. Edward H. Cushing, assistant clinical professor of medicine.
Dr. Harry Hauser, assistant professor of roentgenology.
Dr. William C. McCally, assistant clinical professor of surgery.
Dr. Paul G. Moore, assistant clinical professor of ophthalmology.
Dr. Michael Paul Motto, assistant clinical professor of ophthalmology.
Dr. Harley A. Williams, assistant clinical professor of medicine.

OREGON

New Tuberculosis Hospital. — An allotment of $90,000 from PWA funds, combined with an appropriation by the state legislature, has assured construction of a new hospital for tuberculosis, probably to be located on the campus of the University of Oregon Medical School, Portland. This will be the third state hospital for tuberculous patients.

PENNSYLVANIA

Personal. — The Ex-Residents Association of the Harrisburg Hospital at its recent annual reunion honored Dr. John B. McAlister with a dinner celebrating the fiftieth anniversary of his internship. Judge John E. Fox of the Dauphin County Court served as toastmaster and the speakers were Drs. Henry D. Jump and David Riesman, Philadelphia; James M. H. Rowland, Baltimore, and Henry W. A. Hanson, D.D., president of Gettysburg College, Gettysburg. Dr. McAlister graduated from the University of Pennsylvania School of Medicine in 1887.

TENNESSEE

Changes in Health Officers.—Dr. W. T. Rainey, formerly of Brownsville, has been appointed health officer of Lake County, succeeding Dr. James P. Moon, Tiptonville, who, it is reported, will become a member of the unit in Dyer County. Dr. Earl P. Bowerman, Trenton, has been named health officer of Gibson County. Dr. J. W. Erwin, Savannah, health officer of Hardin County, has been appointed health officer of Giles County to succeed Dr. Wilfred N. Sisk, Pulaski, who went to Johns Hopkins University School of Medicine, Baltimore, for a course in venereal diseases.

TEXAS

Personal.—The Tarrant County Medical Society gave a barbecue and picnic recently in honor of Dr. Leopold H. Reeves, Fort Worth, president-elect of the Texas State Medical Association, at the Lake Worth home of Dr. Thomas B. Bond. Dr. Robert G. Baker, Fort Worth, presided; Drs. Ernst W. Bertner, Houston, president of the state association, and John H. McLean, Fort Worth, made addresses and Dr. Caleb O. Terrell, Fort Worth, on behalf of the society, presented a traveling bag to Dr. Reeves.

Society News.—The Texas Club of Internists will visit Cleveland September 6-10. A program will be presented September 6-7 at the Cleveland Clinic and September 8-10 at the Lakeside Hospital and Western Reserve University School of Medicine.——Drs. William I. Southerland and George K. Stephens Jr., Sherman, addressed the Grayson County Medical Society, Sherman, June 14, on "Diagnosis of Heart Disease" and "Abdominal Pains in Children" respectively.——Dr. Frank Smith Hale, Houston, addressed the Jefferson County Medical Society, Port Arthur, in June on "Hydatid Mole and Chorio-Epithelioma."——At a meeting of the Taylor-Jones Counties Medical Society, Abilene, June 14, Dr. Victor E. Schulze, San Angelo, spoke on "Problems in Diabetes."——Drs. Martin H. Benson and Pauline A. Miller, Lubbock, addressed the Lubbock-Crosby Counties Medical Society in Lubbock June 7 on "Parenteral Infections Causing Diarrhea in Infants" and "Diarrhea in Infants and Young Children" respectively.

UTAH

Committee on Industrial Health. — The council of the Utah State Medical Association appointed a committee on industrial health, July 25, consisting of Drs. Oza J. LaBarge, chairman, Salt Lake City; Paul S. Richards, Bingham Canyon, and John R. Anderson, Springville.

WASHINGTON

Fraternal Order Seeks to Coerce Physicians. — At a recent state convention of the Fraternal Order of Eagles, a resolution was adopted providing that committees will call on representatives of medical organizations throughout the state to learn whether or not they will allow their members to act as physicians for the local Eagle organizations. If this procedure is disapproved by the medical societies, it is expected that the Eagles will vigorously support measures for socialization of medicine, *Northwest Medicine* reports.

WEST VIRGINIA

Changes in State Health Department.—Dr. Albert M. Price, Charleston, formerly director of county health work in the state department of health, has been appointed collaborating epidemiologist and director of the division of communicable diseases. Dr. Thomas H. Blake, Charleston, director of the division of maternal and child hygiene, succeeded Dr. Price in the county health work and Dr. Thomas W. Nale, Charleston, assistant to Dr. Blake, succeeded him.

Society News.—Dr. James R. Bloss, Huntington, addressed the Cabell County Medical Society, Huntington, July 21, on "Some Phases of Medical Economics." —— Drs. Charles E. Conrad, Harrisonburg, Va., and Orlando S. Reynolds, Franklin, addressed the Potomac Valley Medical Society at a meeting at Thorn Spring Park near Franklin June 23 on "Pediatric Problems of Special Interest to the Practicing Physician" and "Analgesia in Labor" respectively.——Dr. Joseph H. Barach, Pittsburgh, addressed the Wetzel County Medical Society, New Martinsville, June 30, on "A Scientific Approach to the Treatment of Diabetes."

Kanawha Society Opposes Regimentation of Physicians.—The Kanawha Medical Society through its executive board has recorded its opposition "to any and all plans which may be presented to the congress of these United States for enactment into law which will tend toward the regimentation of the physician or the patient." A resolution expressing disapproval of the plan of action outlined at the National Health Conference at Washington, D. C., July 18-20, was adopted at a recent meeting. The resolution also reaffirmed "the traditional spirit of willingness of our profession to continue to do freely and well all proper charity work which comes to us."

WISCONSIN

Personal.—Dr. Benjamin Lieberman has resigned as director of school hygiene in the Milwaukee Health Department to become director of health service at the Milwaukee State Teachers' College.——Dr. Joseph F. Smith, Wausau, received an engraved plaque as a gift from the Ninth Councilor District Medical Society commemorating twenty-five years of service as the society's secretary. The plaque was presented at the summer meeting June 30 in Marshfield.

District Meetings.—At the annual meeting of the Fifth Councilor District Medical Society in Sheboygan June 30 the speakers were Drs. Paul B. Magnuson, Chicago, on medical and surgical treatment of arthritis; William F. Lorenz, Madison, blood tests for syphilis; Walter Schiller, Chicago, cancer of the cervix, and Cleveland J. White, Chicago, who held a clinic on diseases of the skin. Drs. Willard O. Thompson, Chicago, and George R. Dunn, Minneapolis, addressed the Ninth Councilor District Medical Society June 30 on "Practical Phases of Endocrine Treatment" and "Treatment of Fractures" respectively.

HAWAII

Society News.—Dr. Wilhelm Dressler, Vienna, recently lectured before the Honolulu County Medical Society on clinical cardiology, elementary and advanced electrocardiography. Dr. Albert Graeme Mitchell, Cincinnati, gave a series of refresher lectures on pediatrics under a maternal and infant hygiene program of the territorial board of health, speaking on the islands of Hawaii, Maui and Kauai as well as in Honolulu. Dr. Bruce H. Douglas, Detroit, has been in the islands during the summer making a survey of the tuberculosis situation.

GENERAL

Medicolegal Conference.—The Massachusetts Medico-Legal Society is sponsoring a two day conference to be held October 4-5. Physicians and lawyers interested in medicolegal work are invited to attend; registration will be requested although no fee will be charged. The tentative program covers technic and demonstrations of postmortem examinations, discussion and demonstrations of such topics as identification, finger prints, ballistics and medicolegal chemical tests, and lectures on medicolegal laws and procedures and the physician as a medical expert. Dr. William H. Watters, 270 Commonwealth Avenue, Boston, is chairman of the committee in charge of arrangements.

Fellowships in Psychiatry.—The National Committee for Mental Hygiene announces a group of appointments for one year's training in extramural psychiatry. Under a grant from the Commonwealth Fund the following have been appointed:

Dr. Grace E. McLean, Pilgrim State Hospital, Brentwood, N. Y., to the Cleveland Child Guidance Clinic.
Dr. John A. Rose, Cornell University Student Health Service, to the Philadelphia Child Guidance Clinic.
Dr. John Russell, Osawatomie (Kan.) State Hospital, to the Los Angeles Child Guidance Clinic.
Dr. Rex E. Buxton, Iowa State Psychopathic Hospital, Iowa City, to the Judge Baker Guidance Center, Boston.
Dr. William B. Curtis, Bellevue Hospital, New York, to the Mental Hygiene Clinic, New York.

Under local provision Dr. William L. Holt Jr., Worcester State Hospital, Worcester, Mass., was assigned to its child guidance clinic and Dr. Norman Westlund, Traverse City (Mich.) State Hospital, to the Children's Center, Detroit.

Award in Industrial Medicine.—At the annual meeting of the American Association of Industrial Physicians and Surgeons in Chicago in June, announcement was made of the establishment of the W. S. Knudsen Award "for the most outstanding contribution to industrial medicine." The award, a bronze plaque, is the gift of William S. Knudsen, president of General Motors Corporation, and members of the committee on award of the association include Drs. Loyal A. Shoudy, chief of medical service, Bethlehem Steel Company, Bethlehem, Pa., chairman; McIver Woody, medical director, Standard Oil Company, New York, and Clare F. N. Schram, Kingsport, medical director, Tennessee Eastman Corporation. The first award will be presented at the association's annual meeting in 1939.

Bequests and Donations.—The following bequests and donations have recently been announced:

Mount Sinai Hospital, New York, $10,000 at termination of a trust established in the will of the late Mrs. Tessie K. Frank.
Roosevelt Hospital, New York, $5,000 by the will of the late Mrs. Elizabeth Newcomb.
Mount Sinai Hospital, Philadelphia, $1,000 by the will of the late Jacob Notkin.
St. Agnes Hospital, Philadelphia, $500 from the estate of the late Dr. John J. Fralinger to maintain a bed for needy persons.
Jewish Hospital, Brooklyn, $5,000 by the will of the late Simon F. Rothschild.
Michael Reese Hospital, Chicago, $15,000 by the will of Dr. Emanuel Friend. At the termination of several trusts the hospital will receive funds for a convalescent home; if it does not accept the home the funds will go to the Albert Merritt Billings Hospital, Chicago.
Jefferson Medical College, Philadelphia, will be the final beneficiary of a trust fund of $60,000 created by the late Dr. Warren C. Batroff.
Mount Sinai Hospital, New York, $50,000; Beekman Street Hospital, New York, $5,000 by the will of the late Joseph F. Cullman.
Jewish Hospital, Brooklyn, $15,000, and Lenox Hill Hospital, $1,000 by the will of Mrs. Rose Abraham.

Association for Study of Neoplastic Diseases.—The annual meeting of the American Association for the Study of Neoplastic Diseases will be held at the Mayflower Hotel, Washington, D. C., September 8-10. The meeting will be mainly a lantern slide and x-ray film demonstration. Sessions will be devoted to the following subjects: lesions of the stomach, colon and rectum, under the chairmanship of Dr. George A. Stewart, Baltimore; lesions of the pancreas and small intestine, Dr. Janvier W. Lindsay, Washington, D. C.; endocrinology as related to neoplasia, Dr. Charles F. Geschickter, Baltimore; lesions of the oral cavity, larynx, trachea and lungs, Dr. George R. Moffitt, Harrisburg, Pa.; mediastinal and retroperitoneal tumors, Dr. Louisa E. Keasbey, Lancaster, Pa.; lesions of the breast, Dr. John Shelton Horsley, Richmond, Va., and lesions of the bones, Dr. Ralph E. Myers, Oklahoma City. Dr. Leopold Clarence Cohn, Baltimore, is president of the association and Dr. Eugene R. Whitmore, Washington, secretary.

Southern Tuberculosis Meeting.—The annual meeting of the Southern Tuberculosis Conference and Southern Sanatorium Association will be held in Louisville, Ky., at the Brown Hotel September 19-21. There will be medical and nonmedical sections as well as general sessions. Among the medical speakers will be:

Dr. Frederick T. Lord, Boston, Certain Aspects of the Program in Massachusetts for the Prevention and Control of Tuberculosis.
Dr. James Burns Amberson Jr., New York, The Future Possibilities of the Tuberculosis Problem.
Dr. Porter P. Vinson, Richmond, Va., Tuberculous Tracheobronchitis.
Dr. John Alexander, Ann Arbor, Mich., Role of Lobectomy and Pneumonectomy in Bronchiectasis and Carcinoma of the Lung.
Dr. Kendall Emerson, New York, The Responsibility of the National Tuberculosis Association for State and Local Programs.

At the conference banquet Monday night the speakers will be Drs. Henry Chesley Bush, Livermore, Calif., president of the National Tuberculosis Association; Henry G. Reynolds, Paducah, Ky., president of the Kentucky State Medical Association, and Arthur T. McCormack, Louisville, president of the American Public Health Association. Dr. Paul H. Ringer, Asheville, N. C., is president of the conference and Dr. Jesse D. Riley, State Sanatorium, Ark., of the sanatorium association.

Obstetricians, Gynecologists and Abdominal Surgeons.—The fifty-first annual meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons will be held at the Greenbrier Hotel, White Sulphur Springs, W. Va., September 22-24. Among the speakers will be:

Dr. Otto S. Krebs, St. Louis, Sterility Studies.
Dr. Albert Mathieu, Portland, Ore., Recent Developments in Diagnosis and Treatment of Hydatidiform Mole and Chorio-Epithelioma.
Dr. Emil Novak, Baltimore, Clinical Syndromes Referable to Disorders of Ovulation.
Dr. Emmett D. Colvin, Atlanta, Ga., Behavior of Basal Metabolism in the Course of Developing Toxemia of Pregnancy: Correlation with Placental Infarcts and Other Significant Findings.
Dr. Thomas R. Goethals, Boston, Management of Breech Delivery in Primiparae.
Dr. John C. Hirst, Philadelphia, Maternal and Fetal Expectations with Multiple Pregnancy.
Dr. Jacob P. Greenhill, Chicago, Increased Incidence of Fetal Abnormalities in Cases of Placenta Praevia.
Drs. Virgil S. Counseller and Nelson W. Barker, Rochester, Minn., Postoperative Thrombophlebitis: Prevention and Treatment.

The Joseph Price Oration will be delivered by Dr. Charles Burger, professor of obstetrics and gynecology, University of Budapest, Hungary. Dr. Paul Titus, Pittsburgh, president of the association, will give his official address on "Obstetrics and Gynecology as a United Specialty."

Government Services

Health Activities Under Social Security Act

The U. S. Public Health Service recently issued a summary of its activities during the three years since the Social Security Act became a new law, providing an annual appropriation of $8,000,000 for the development of public health work.

Nearly 3,000 persons had received postgraduate training in public health work up to June 30, 1937, and 1,300 more have been in training in 1938. They include 651 medical officers, 162 engineers, 1,540 nurses, 451 sanitation officers, eighty-eight laboratory workers and sixty others. More than 200 medical officers had had a full year's course in public health administration. Public health nurses employed by local and state agencies increased from 16,000 to 18,000. State health departments employed 322 health nursing administrators, supervisors and consultants in 1937, compared with 149 in 1931. Six states are completely covered by full-time health officers; in some states several counties are combined into districts.

Through grants-in-aid to states, a number of specialized health activities have been developed as separate divisions of state health departments. By July 1, 1937, twenty-four states had separate divisions for venereal disease control compared with thirteen before the new law; thirty had full time and two part time officers for venereal disease control. Fifteen states now have separate divisions for industrial hygiene, compared with three prior to Jan. 1, 1936. Other separate divisions have been set up for local health administration, public health nursing, maternal and child health, dental hygiene, public health education, engineering, tuberculosis, cancer control, laboratories, malaria control and rodent plague control.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 13, 1938.

New Sources of Ephedrine

Ephedrine is obtained from herbs which grow wild in China and in Spain. No ephedrine has been obtained from Spain since the civil war began, and the small district of China in which the herb grows was the scene of hostilities in the early part of the Japanese invasion, so that even the part of the crop which was not trodden under foot by the troops could not be collected. The result was that the price of ephedrine soared and a famine was threatened; but this has been averted in the following way. The drug was produced synthetically in Europe and an Indian herb which also is a source of ephedrine but had been rejected by the manufacturers because its content of ephedrine was far below that of the Chinese herb is being used. London dealers are eager to buy the Indian herb, which previously was fed to pigs. The result is that the price of ephedrine has dropped from four times the normal to only 25 per cent above it. The experimental cultivation of the herb has been begun in the British colony of Kenya by means of material supplied from the Kew botanical gardens. The cost of producing ephedrine synthetically is stated to be well above the market price of the natural product when the Chinese plant is available.

The Fight Against Cancer

At a meeting of the British Empire Cancer Campaign, Sir Arthur MacNalty, chief medical officer of the Ministry of Health, stated that 65,000 deaths took place annually from cancer. It had now taken the second place in the list of fatal diseases in this country. From the beginning of our national records of mortality each year had shown, almost without exception, a rise in the number of deaths from this cause. The increasing longevity of the population was an important factor, since the mortality from cancer was greater at the higher ages. Today people lived on the average fifteen years more than they did a generation ago. The ability to diagnose cancer in difficult cases had been steadily improving. The highly complex study of the causes of cancer was being carried on with great vigor throughout the world and British scientists were contributing their full share. In diagnosis and treatment the outlook was brighter than it was. In Great Britain twenty-two radium centers, which were specialized institutions both for diagnosis and for treatment, were established within recent years.

Lady Barrett (gynecologic surgeon) gave statistics of a London cancer clinic. Of patients with early cancer treated more than five years ago, 83 per cent were alive and well today. Patients treated later, when the disease was more advanced, gave a figure of 65 per cent. Of all the patients treated, 35 per cent were alive at the end of five years. These figures showed that if patients could be induced to seek treatment in the early stage there was a very good hope of complete cure.

Hospitals for Air Raid Casualties

The Ministry of Health is working out comprehensive plans for the hospital accommodation of air raid casualties and has issued a circular to the local authorities to the effect that every hospital must be prepared to deal with air raid casualties occurring in its immediate neighborhood. Also every hospital which is not in a specially dangerous position will be expected to receive both casualties and ordinary patients from dangerous areas. The plans which have been made would be put into immediate operation in various parts of the country should the necessity arise. It is a shocking result of modern warfare that hospitals, formerly a refuge for the wounded, should now themselves be a dangerous place for them.

PARIS

(From Our Regular Correspondent)

July 30, 1938.

Chair of Endocrinology in Collège de France

The Collège de France is an institution devoted chiefly to research in medicine and all other branches of science. Some of the most eminent men in France have been members of its faculty, which is independent of the Faculté de médecine, although both organizations form part of the University of Paris. The minister of public education has just announced the creation of a chair of endocrinology in the Collège de France and has appointed as its first occupant Professor Courrier of Algiers, whose investigation of the biology of the female sex hormones in their relation to the hypophysis in 1937 was of great interest.

Two Eminent Teachers Become Emeritus Professors

The law which now requires the retirement of university professors at the age of 65 was modified several years ago in favor of some distinguished members of French faculties of medicine so that they would not be obliged to retire until they had reached the age of 70. This prolongation of the age of retirement enabled two Paris clinicians, well known all over the world, to continue their teaching activities until the end of the 1937-1938 school year. The two professors who have now reached the age limit are Professor Bezançon, phthisiologist, and Professor Marion, urologist. The clinics of these two teachers have been visited by many American specialists.

Sulfanilamide Treatment of Streptococcic Meningitis

Three papers were read at the June 17 meeting of the Société médicale des hôpitaux of Paris in which ten cases of streptococcic meningitis successfully treated with sulfanilamide were reported. In the first paper Dr. Brulé and his associates reported a case of acute optochiasmatic arachnoiditis with streptococcic meningitis, which had developed after the lesion of suppurative tonsillitis had evacuated its contents spontaneously about three weeks before the patient's admission to the hospital. During the first stage the only complaint was a severe headache. There was a slight rise of temperature, but ocular examination revealed the typical appearances of acute optochiasmatic arachnoiditis secondary to the tonsillar infection. At this time lumbar puncture showed 240 leukocytes per cubic millimeter. In the second stage (three days after admission) the symptoms and signs of diffuse meningitis became marked. Cultures of the fluid obtained by lumbar puncture showed the causative organism to be the hemolytic streptococcus. Sulfanilamide was immediately given, 65 Gm. by mouth and three intraspinal injections of 0.2 Gm. over a period of twenty-eight days. The authors expressed the opinion that the intraspinal method of administration had been more efficacious than the oral method. During the third stage a marked improvement of the arachnoiditis was noted. This is unusual, because as a rule this condition ends in complete loss of sight.

The second paper was by Dr. René Martin of the Institut Pasteur, who stated that the mortality rate of streptococcic meningitis had until recently been 97 per cent. He had given sulfanilamide to three children with the disease, all of whom recovered. In addition to these three children observed at the Institut Pasteur, three others with streptococcic meningitis of otitic origin had been successfully treated with sulfanilamide. The drug should be given in large doses and the administration continued for at least several weeks after apparent recovery to

prevent recurrences. During the first few days sulfanilamide is given both by mouth and intraspinally. For oral administration, adults are given from 8 to 10 Gm. and children 0.15 Gm. daily per kilogram of weight. On account of rapid elimination of the drug, it is advisable to give it every two hours during the day and every three hours during the night. It is given intraspinally during the first days of the illness. After from 10 to 20 cc. of spinal fluid, according to the age of the patient, has been withdrawn, an equal quantity of an 0.85 per cent solution of sulfanilamide, previously heated to body temperature on a water bath, is injected. The doses for intraspinal use are increased or decreased according to whether the concentration of the sulfanilamide in the spinal fluid is superior or inferior to 4 mg. per hundred cubic centimeters of the cerebrospinal fluid. The higher the concentration, the more rapidly does recovery take place. The permeability of the meninges toward sulfanilamide varies with each patient; hence the necessity of adjusting the doses for intraspinal use according to the concentration of sulfanilamide in the cerebrospinal fluid. Dr. Martin expressed the opinion that the administration of sulfanilamide by the intraspinal route was the chief factor in the success of the treatment in his cases of streptococcic meningitis.

The third report was submitted by Prof. Robert Debré and his associates. Before using sulfanilamide, they had observed twenty similar cases of meningitis with but one recovery. The three patients to whom they gave sulfanilamide were children 6, 4 and 9 years old and in all the meningitis was of otitic origin. These authors employed both the oral and the intraspinal method of giving the drug. For oral administration, doses as high as from 3 to 5 Gm. daily must be given even to children, and they must continue to be given for three weeks after apparent recovery. For intraspinal administration they used an 0.85 per cent solution, of which a minimum of 15 cc. should be injected if the concentration of sulfanilamide in the spinal fluid is not inferior to 4 mg. per hundred cubic centimeters. When this concentration is reached or when the spinal fluid is sterile and contains very few leukocytes, the intraspinal method is discontinued. The spinal fluid became sterile within forty-eight hours after the beginning of treatment. The complications noted, so far as the effects of the drug are concerned, were cyanosis, at times very marked at the onset but decreasing noticeably even though use of the drug was continued, a rather persistent cough and in one case a drop in the red cell count to 1,730,000.

BERLIN

(From Our Regular Correspondent)

July 14, 1938.

Blindness Defined

The National League for Industrial Employment of the Blind has established, with governmental approval, certain practical definitions of blindness, designed to facilitate classification of virtually blind persons. In addition to the totally blind, all persons are considered as blind whose central visual acuity amounts to from one fiftieth to one twenty-fifth of the normal (although most persons of the latter group are able to find their way about the streets without the help of others). Practical blindness may also be considered present even if the visual acuity is greater than one twenty-fifth of normal, in special cases, as for example if a depreciated acuity of vision is accompanied by considerable diminution of the visual field. The latter class is composed chiefly of patients who present certain disorders: optic atrophy, glaucoma, pigmental degeneration, retinal detachment, hemianopia. Further particular conditions in which blindness may be assumed are nystagmus with phantom movements of external objects perceived. nyctalopia following pathologic changes of the inner eye, and finally cases in which a full practical evaluation of central visual acuity is qualified by the advanced age of the patient.

Child Labor and the Protection of Youth

New legislation to regulate child labor and the working hours of adolescents went into effect April 30. The new statute, which bears the title "Youth Protection Law," embodies the following principles: Child labor is generally forbidden. The adolescent worker is protected by a curtailment of working hours and prohibition of such night work as would make excessive demands. Sufficient leisure time is assured for further vocational training, physical exercise, development of character and national political education. In addition it is provided that the adolescent worker shall have vacations and that the latter may be purposefully utilized. Any person under the age of 14 is legally considered a child. Adolescents are defined as persons over 14 but under 18 years of age. Special regulations are envisaged which apply to certain occupational fields such as domestic service, agriculture in its various branches, fishing, maritime and inland navigation, and aviation.

It was difficult to formulate a legal definition of "work," but a clear understanding of what is meant by the term is particularly important with relation to child labor. Accordingly the new law concerns not only occupation in the apprentice relationship or in the employee relationship but also those services, which resemble such relationships. To avoid difficulties, it is stipulated that school children 12 years old and over may be employed at light tasks in commercial establishments and act as errand runners and as assistants in sports. So-called family industries are not exempted from the provisions of the child labor laws, so the legal protection of the child extends into this sphere. Certain exceptions are allowed under state control. Children 12 years of age and over are permitted to work under the strictest state supervision and a precise record of the hours put in is kept on a special time card. This procedure is followed even if only one child is involved. This authorized employment of children is restricted as follows: The work period must not exceed two hours daily during the school year or four hours daily during vacation. Working hours must lie between 8 a. m. and 7 p. m. but not prior to morning school hours. Time required for traveling to and from work must fall within the stipulated time limits, namely must not extend beyond 7 p. m. The law further guarantees an uninterrupted free period of at least two hours following morning school hours and a similar period of at least one hour following afternoon school hours. During school vacations the child must be permitted at least fifteen days, consecutive if possible, of absolute freedom from work. Children may not work on Sundays and holidays excepting as helpers in sports. Children may perform only certain duties such as arrangement of merchandise, and delivery and messenger services. Exceptions are permitted in the theatrical and cinema industries. Special provisions govern infant entertainers under 3 years of age. Adolescent workers may work a maximal eight hour day and forty-eight hour week. Class hours in trade schools are reckoned as a part of working time. At the close of the working day an uninterrupted rest period of at least twelve hours must be assured. Certain rest periods are required if the working hours are long. Adolescents must not as a rule be employed at night work between the hours of 8 p. m. and 6 a. m. Certain exceptions are made in the case of employees of hotels, bakeries and the theatrical and allied industries. Other exceptions with regard to night work concern industries which are worked in shifts. Adolescent workers may no longer work after 2 p. m. on Saturdays, with certain exceptions; employees of transportation services, the food industry, hairdressing industry and so on. Now for the first time employers are compelled by law to provide adolescent workers vacations with pay. Accordingly, adolescents under the age of 16 are entitled to fifteen vacation days, workers from 16 to 17 years of age are entitled to twelve days or, if part of the time is spent in a Hitler Youth Camp or excur-

sion, to eighteen days. The new statute is implemented with extremely rigorous penalties for violation of its provisions. An unscrupulous employer who permits an employee under 18 years of age to risk serious endangerment of health from overwork is liable to a minimal jail sentence of three months.

BUENOS AIRES

(From Our Regular Correspondent)

July 30, 1938.

Department for Study of Allergic Diseases

A department for the study of allergic diseases, especially pollinosis, was organized some months ago in the Hospital Municipal de Vicente López in Buenos Aires. Dr. J. A. Bozzola, head of the department, made studies on the subject in the United States. He has recently made several studies on the subject in Argentina. He made determinations of the density of the pollen in the air in the various seasons of the year. He also studied the plants which produce pollen. The department has an office for consultations, a laboratory for the preparation of allergic extracts, and gardens for cultivation of plants to be used in preparing the extracts.

A new department for studies of allergic diseases is going to be opened in the near future in the Hospital de Clínicas of the Faculty of Medicine of Buenos Aires.

Rapid Diagnosis of Diphtheria

Dr. Alfredo Sordelli, head of the Instituto Bacteriológico del Departmento Nacional de Higiene, recently presented an interesting article of his collaborator Dr. Alfredo Mansullo to the members of the Academia Nacional de Medicina. The article deals with a method for the diagnosis of diphtheria by which the diphtheria bacillus can be cultured in three hours and a macroscopic and microscopic diagnosis of the colonies made at the same time. A mixture is prepared with 15 cc. of meat broth with peptone, 1.5 cc. of defibrinated ox blood and 1.5 cc. of a 2 per cent solution of potassium tellurite. The pharyngeal exudate is collected with a cotton swab and the latter is moistened with 2 cc. of the liquid mixture, placed in a test tube and left during three hours at a temperature of from 36 to 38 C. Small characteristic black colonies can be observed in the swab at the end of three hours, when the exudate contains diphtheric bacilli. Stained preparations, growths and inoculation of guinea pigs can be done with the black colonies. Carriers of diphtheria bacilli can be detected by the technic, which makes possible the examination of hundreds of children in a single forenoon. A still more rapid method consists in moistening the pseudomembranes with a 2 per cent solution of sodium tellurite. Ten minutes later the throat is examined. When the exudate is diphtheric the membrane has become black or gray. The results of the method were compared with those of the cultural method in the department of diphtheria of the Muñiz Hospital. In most cases of diphtheria the results of the test were positive, whereas negative results were obtained in all cases in the absence of diphtheria.

Role of Adrenals in Hypophysial Diabetes

Investigations which have been carried on by Collip, Evans and Long have failed to produce hypophysial diabetes in normal animals. According to Houssay the failure is due to a lack of precaution, as the hypophysial glands have to be collected on solid carbon dioxide and the extracts have to be prepared and kept at a low temperature. Both the hypophysial glands and the extracts become inactive in a few hours if they are kept in a warm temperature. A hyperglycemia of from 0.15 to 0.38 per hundred cubic centimeters of blood which lasts all day may be obtained in from three to five days by using well prepared hypophysial extracts. Hyperglycemia diminished after injections of hypophysial extracts. Whenever it diminishes, the administration of increased doses of the extract induces a new increase and later on a permanent diabetes, which persists after the injections are discontinued (Young). Houssay and his collaborators proved in 1929 and also by further studies on the subject that the resistance to insulin increases earlier than glycemia while the injections of hypophysial extracts are being given. The secretion of insulin by the pancreas is greatly diminished in animals with induced hypophysial diabetes. When diabetes of this type is permanent, the islands of Langerhans show degeneration. The theory concerning the part taken by the adrenals in transmitting the diabetogenic action of the anterior lobe of the hypophysis has been generally accepted since the reports by Long on the subject. Houssay and Biasotti in 1933 and in 1936 and Houssay and Leloir in 1935 found that the grafting of an anterior lobe of the hypophysis in toads without adrenals or pancreas and with or without a hypophysis intensifies attenuated diabetes. Houssay and Biasotti recently induced anterohypophysial diabetes in dogs. The animals were first deprived of an adrenal, then of the pancreas except for a remaining 4 Gm. of the structure, and at last of the remaining adrenal gland, after which an injection of the anterior lobe of the hypophysis was made in the peritoneum of the animals, which were maintained in the course of the experiment by means of certain doses of adrenal cortex extract, sodium citrate and sodium chloride. Hyperglycemia of 0.155, 0.175 and 0.25 was induced in dogs in this condition within three or four days of the administration of the anterohypophysial injection. Small doses of anterohypophysial extract which are not toxic may be used successfully after partial resection of the pancreas. The injections of adrenal cortex extract administered alone have no action. The results of these experiments show that the diabetogenic action of the anterior lobe of the hypophysis does not take place through the adrenals and that hypophysial diabetes can be induced in dogs which have previously been deprived of their adrenals. Adrenotrope extracts and prolactin fail to induce diabetes in dogs previously deprived of the hypophysis and of most of the pancreas. Dogs in the last mentioned condition have a normal glycemia. The administration of a dose of from 20 to 40 mg. of fresh anterior lobe of the hypophysis of bovine animals for each kilogram of body weight of the dogs induces hypophysial diabetes in the latter.

AUSTRALIA

(From Our Regular Correspondent)

July 20, 1938.

Health Insurance

Although there is still some anxiety among practitioners as to the effects of national insurance, the general excitement which accompanied the passage of the bill through parliament has passed, and it is now possible to review the situation more clearly. Some form of health insurance was inevitable for Australia. This country has not escaped the economic developments taking place all over the world and cannot remain blind to the fact that greater specialization in industry and the accumulation of capital in the hands of the big industrial concerns has reduced private production and greatly increased the number of wage earners in the community. Wages are cut to a minimum in the majority of cases, with the result that little provision can be made against the mischances of life or the financial stress occasioned by ill health. Unless medical services are to be put on a charitable basis, some form of compulsory insurance is necessary. At the same time "industrialization" is invading the medical field. The extensive knowledge and rapid development of medical science render specialization imperative. Moreover, overhead costs of an individual private practice, when viewed together with the decreased purchasing power of the greater part of the community, are fast becoming prohibitive. The practice of medicine is the most personal of the professions, and for this reason perhaps it has remained individual for so

long; but we have now reached a stage in the development of our society at which efficient service can best be achieved by a coordination of individual effort. Such a coordinated service is at present available to only a small section of the community.

Some reorganization of health services then is socially necessary; but whether the Australian government has provided this in the most desirable form, from the point of view either of the public or of the medical profession, is a debatable question. The bill which has just been enacted provides a general practitioner service for all wage earners whose income does not exceed £365 per annum in return for a weekly contribution shared equally by employer and employee. Provision has been made also for the voluntary inclusion of dependents of compulsory contributors. Thus over 80 per cent of the population is affected. No provision is made, however, for unemployed workers (about 5 per cent of the population) or for those small farmers and business men whose income is less than £365. Moreover, the health service provided is considered by many to be totally inadequate and to consist mainly of what the community in the past was best able to afford. Insurance makes available to contributors a general practitioner service, together with prescribed medicines, drugs and certain surgical appliances. Extra fees are payable for maternity services, major operations, laboratory tests and any specialist services. Thus the most efficient medical service still remains available to only a small section of the community.

From the point of view of the medical profession also national insurance as at present constituted is open to serious criticism. Members of the British Medical Association in Australia have clearly demonstrated that the capitation fee as originally proposed by the government is inadequate remuneration for the work it would entail. A royal commission has now been appointed by the government to investigate fully the financial aspect of the general practitioner's case. The only way in which a practitioner could maintain his present income, should the original proposals be put into operation, would be to build up a large panel. This however, has three disadvantages: he could do so only at the expense of his neighbor, at the expense of his health and at the expense of his own efficiency. The introduction of national health and pensions insurance in Australia therefore, although it will relieve the commonwealth government of a tremendous expenditure in pensions payments, has done little to provide a more efficient health service for the community as a whole.

Chemical Composition of Australian Foods

Until the present, those who wished to calculate the calorific equivalents, vitamin content or other quantitative aspect of diets in Australia have been restricted to figures published by American or English investigators. There have just been published, however, in the fifth report of the Commonwealth Advisory Council on Nutrition, the results of an extensive analysis of Australian foods for water, ash, protein, fat, carbohydrate and fiber content. As to calories, there are no very profound differences between Australian foods and foods overseas. The values for the protein of Australian breads (and of cereals generally) are shown to be lower than English and American figures, and meat also tends to have a low protein content in comparison. Dairy products show no appreciable differences, but the protein content of Australian vegetables and fruits is in most cases higher than that of other countries. On the basis of these analyses there has been drawn up an "economic index of foods," designed to function in times of national emergency, such as war or severe depression, which represents a compact summary of knowledge as to which foods contain the cheapest calories. Supplementary to this index is a list showing the amount of protein, fat and carbohydrate available for one penny in the case of some 214 foodstuffs. No account has been taken at this stage of mineral or vitamin content.

MINERAL IMBALANCE

In view of the fact that there exists in Queensland considerable evidence of a mineral imbalance in human beings, a series of analyses was carried out to determine the mineral content of some Queensland foods. The analytic results showed no especial deficiencies. While this allows attention to be paid to the question of supply and consumption, with an added sense of security, one physiologic aspect remains for consideration, and that is the question of variations in gross mineral requirements occasioned by altered habits or environments.

Immunity Reactions of Viruses

Dr. F. M. Burnet, whose contributions to the literature of filtrable viruses are both numerous and valuable, has carried out further research on the immunologic reactions of viruses and, in collaboration with E. V. Keogh and Dora Lush, working at the Walter and Eliza Hall Institute of Medical Research in Melbourne, has recently written a monograph on this subject. These workers consider that both plant and animal viruses can be most usefully considered as minute, organized, living microorganisms, at all events as far as the problems of immunity are concerned; and it is pointed out that, despite certain superficial differences due to the smaller size of the viruses, there is no real difference between the behavior of viruses and that of bacteria in their neutralization reactions with antiserums. The study of neutralization reactions of the filtrable viruses has been difficult in the past, as titration of viruses in the living animal is at best inexact. Burnet has shown, however, that the chorio-allantoic membrane of the developing egg provides a means of virus titration of much greater accuracy than the animal, and he and his colleagues in Melbourne have made use of this method in the investigation of a number of animal viruses and their antiserums.

Accumulation of data by the egg membrane technic has enabled these workers to attempt an analysis of virus neutralization reactions. They have shown that the viruses of vaccinia, influenza, louping ill, laryngotracheitis of fowls, Newcastle disease of fowls and rabbit myxomatosis conform in their reactions more or less closely to a hypothetic ideal case. This case was developed on the assumption that virus and antibody combined reversibly and that the infectivity or lack of it of a given virus particle was determined by the amount of antibody united to it at the time of effective contact with the susceptible cell. Each virus studied in detail showed some points of individuality, but all showed a general conformity with the broad outlines of the ideal case. On the basis of these data, Burnet and his co-workers have interpreted the neutralization reaction with animal-pathogenic viruses as follows: Virus inactivation by immune serum results primarily from union of antibody to the virus surface. This union is a reversible one; it takes place at a rate and reaches an equilibrium determined by the ordinary laws of reversible chemical unions. As a result of this union with antibody the virus is hindered from entering susceptible cells or from multiplying should it succeed in reaching that intracellular environment essential to its growth. Certain susceptible cells are protected against infection by lesser degrees of antibody coating on the virus particle than are required by other types of cell. It is shown also that the percentage law, discovered by Andrewes and Elford in the case of the bacteriophages, holds in the case of viruses as well, the reason for this being the relatively enormous amount of antibody to antigen in the neutralization reaction over a large range of antiserum dilutions.

Although this work has theoretical rather than directly practical significance, the monograph concludes with a consideration of the production of active immunity against virus infections. The use of living attenuated virus is held to be the method most likely to give success, the employment of killed virus being considered of little use for this purpose.

DESTRUCTION OF RABBITS WITH VIRUS

The idea that the virus or rabbit myxomatosis might be a possible means of controlling excessive increase in wild rabbit populations is of particular interest to Australia, and the Council for Scientific and Industrial Research is carrying out extensive experiments to ascertain the infectivity of the virus for Australian wild rabbits and to confirm its noninfectivity for other domestic and native wild animals. Although the virus of myxoma has been regarded as the most species specific of all viruses, it has been found that the chorio-allantois of the developing egg is susceptible to its infection, and Burnet's egg membrane technic has offered a single and inexpensive method of quantitative study of what would otherwise be a difficult and expensive investigation. An interesting preliminary epizootiologic observation in connection with rabbit myxomatosis is that the infected rabbit is shunned by his fellows. This will have an unfortunate effect in limiting the spread of the disease and will hinder the biologic control of the rabbit pest in Australia.

BELGIUM

(From Our Regular Correspondent)

July 1, 1938.

Poisoning from Benzene

A law was recently passed by which workers who are exposed to poisoning from benzene in the mirror industry have to report for periodic medical examination. Workers who handle or prepare varnishes which are made up with benzene or its derivatives have to report for medical examination after the first three months they are at work and at intervals of three months afterward. The examination will include counting of the erythrocytes and leukocytes. It is performed by a physician who is chosen by the manager of the industry. The intervals for medical examinations may be shortened if the physician believes it is necessary to do so. The results of the examination will be reported within two weeks to the physician appointed for the protection of workers in the given district. The latter can order discontinuation of work to persons showing symptoms of poisoning from benzene.

Prevention of Tetanus

Mr. Renaux, in a lecture before the Société belge de médecine et de chirurgie du travail, discussed serum prevention of tetanus, certain points of which are still a subject of controversy. The injection of antitetanic serum must be administered in cases of war wounds, wounds contaminated by either the soil or feces and those in which there is a great loss of tissues. However, there are certain cases with apparent exposure of the wounded to tetanus without development of the disease. It is a daily experience to see a benign evolution of wounds which were in danger of contamination by the tetanus bacilli. The development of tetanus in so large a number of cases is exceptional in spite of the fact that the number of cases in which antitetanic serum is administered is small. This experience shows that the body has natural defenses against tetanus bacilli as well as against other bacteria. It shows also that certain general conditions are necessary for the development of tetanus. These conditions are the association of bacteria, underfeeding and depression of the individual. There are also internal and external sources of contamination. An average of from 20 to 35 per cent of persons have tetanus bacilli in the intestine. Laceration of the perineum in the course of parturition is never complicated by tetanus, although in some cases the eventuality of the contamination may have existed. The speaker feels that tetanus does not necessarily develop from contamination of wounds. He said that when the administration of antitetanic serum is indicated it is advisable to desensitize the patient who possibly previously had been given serum.

BUDAPEST

(From Our Regular Correspondent)

July 23, 1938.

Tropical Malaria in Hungary

In recent years tropical malaria has occurred in Hungary with fair frequency. Dr. Paul Végh, clinical assistant in Debrecen, made a special study of this disease, which in Hungary is most frequent from August to November. Last year he observed a good many cases in Debrecen. In the *Orvosi Hetilap* he says that in his cases the first attacks of fever came on after an incubation period of from four to six days. The feverish state is considerably longer than usual in tertian malaria, from thirty to thirty-six hours, and in ten to eighteen hours the pseudocritical fall of the fever can be observed. Then the maximum follows (febris tropica). In his cases the greatest difficulty in differential diagnosis was caused by abdominal typhus. All last year cases were sent to the clinic with the diagnosis abdominal typhus. The great prostration, eventually continuous fever and leukopenia remind one of typhus (the number of leukocytes in our cases was from 3,400 to 7,800). Nevertheless the characteristic monocytosis in the blood picture (from 8 to 19 per cent) should arouse suspicion of malaria, which has to be verified by microscopic examination. Treatment consisted in the administration of atabrine and plasmochin. Although the latter is fairly expensive, it has the advantage of destroying the gametes and in this way recurrences are brought to a minimum.

Resorcinol Poisoning in an Infant

A girl baby, 2½ months old, suffering from summer diarrhea, was given resorcinol 0.05 Gm. in 120 cc. of distilled water for five days. Her condition was aggravated so that her mother took her to the clinic. The patient on admission was very restless and languid. The pulse was 120 and weak. Her lips were cyanotic. The liver was very tender on pressure and even palpation. The spleen was enlarged and painful. The blood was chocolate colored. On treatment her condition made no change to the better. The blood picture showed anisocytosis, poikilocytosis and a few erythroblasts. Suspicion of poisoning arose and the bottle containing the medicine was sent for. It was found that the bottle contained a hundred times the amount of resorcinol prescribed; that is, instead of 0.05 Gm., 5 Gm. had been given. The baby took six teaspoonfuls of the medicine, 1.5 Gm. The baby was given a copious enema, a blood transfusion, oxygen inhalations and physiologic sodium chloride and dextrose solution. The baby recovered and was dismissed from the clinic on the twelfth day after admission.

Marriages

HOWARD W. GOURLIE, Thompsonville, Conn., to Miss Anne MacLeod of River Bennett, N. S., Canada, July 2.

ROBERT T. GRAY, Prospect, Ohio, to Miss Martha Sturgis Cohagen of Zanesville, June 6, at Columbus.

OSMYN WILLIAM MCFARLAND, Hebron, Neb., to Miss Rose Lolita Long of Baton Rouge, La., June 1.

RUDOLF WILLIAM HACK, Momence, Ill., to Miss Willette Mary Drummond of Chicago in July.

PETER JOSEPH PARISI, Basin, Wyo., to Miss Katheryn A. Zietzke of Whitehall, Mont., July 31.

CAMILLE-AIME ROUSSIN to Miss Hortense Olivier, both of Joliette, Que., Canada, June 18.

IVAN WARD GESSLER, McMinnville, Tenn., to Miss Vera Field of Shaw, Miss., in June.

FRANK H. GREEN JR., Rushville, Ind., to Miss Jean Green at Belmont, Mass., July 1.

HARRY GREENBAUM to Miss Sylvia Frankel, both of Jackson, Mich., June 8.

Deaths

Dr. George E. de Schweinitz ✠ president of the American Medical Association in 1922-1923, died at his home in Philadelphia August 22.

Dr. de Schweinitz was born in Philadelphia Oct. 26, 1858, the son of Bishop Edmund Alexander de Schweinitz and Lydia de Schweinitz. He received his A.B. and A.M. degrees from Moravian College in 1876 and his M.D. from the University of Pennsylvania in 1881. After an internship in the Children's Hospital and in the University of Pennsylvania Hospital he served as prosector of anatomy for Dr. Joseph Leidy at the University of Pennsylvania from 1883 to 1886. He also taught therapeutics in the Medical Institute of Philadelphia from 1882 to 1887. He then turned his attention to ophthalmology and became lecturer on medical ophthalmoscopy in the University of Pennsylvania in 1891-1892 and professor of ophthalmology in the Philadelphia Polyclinic and College for Graduates in Medicine, 1891-1893. He was clinical professor of ophthalmology at Jefferson Medical College, 1892-1896, and professor of ophthalmology, 1896-1902. In 1902 he became professor of ophthalmology at the University of Pennsylvania, holding this position until 1924, and then professor of ophthalmology at the Graduate School of Medicine of the University of Pennsylvania from 1924 to 1929. In 1929 he was made professor emeritus of ophthalmology. During the same period he served as consulting ophthalmologist to most of the leading Philadelphia hospitals.

GEORGE E. DE SCHWEINITZ, M.D.
1858-1938

Early in his career he became closely identified with the work of the profession in many different medical societies, including the Philadelphia County, Pennsylvania state and American Medical associations, the Philadelphia Pathological and Neurological societies, the American Academy of Ophthalmology and Otolaryngology and the American College of Surgeons. He was secretary of the Section on Ophthalmology of the American Medical Association in 1891-1892, and chairman, 1896-1897. He served as president of the College of Physicians of Philadelphia, 1910-1913, and of the American Ophthalmological Society, 1916. He was elected an honorary member of the Ophthalmological Society of the United Kingdom and gave the Bowman lecture in 1923. He was also a member of the French, British and Belgian ophthalmologic societies and of all international congresses. As a citizen he was prominent in many affairs, holding memberships on the boards of institutions for the blind and also of the National Institute of Social Sciences and similar groups. In 1924 he was elected a trustee of the University of Pennsylvania and was appointed chairman of its Board of Medical Affairs in 1928.

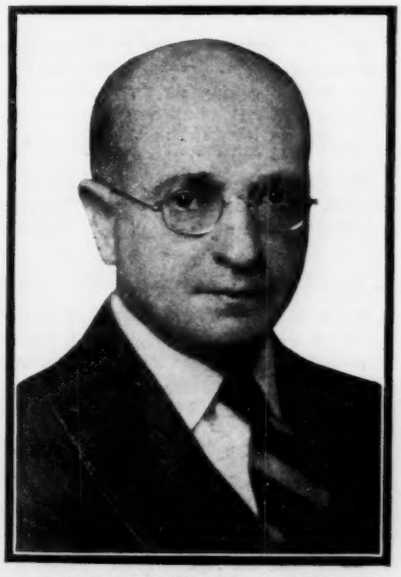
During the World War he was appointed to the Council of National Defense in 1917 and commissioned a major on April 9, 1917, being advanced to lieutenant colonel in May 1918. He was ordered to duty in the Surgeon-General's office in September 1917 and went overseas in October, remaining until March 1918. He was then returned to the Surgeon-General's office as officer in charge of ophthalmology and established the School of Ophthalmology in the Medical Officers' Training Camp at Fort Oglethorpe. At the end of the war he was appointed consultant in ophthalmology and made a member of the editorial board of the medical history of the war. In April 1919 he was commissioned colonel and in 1922 brigadier general in the Medical Reserve Corps.

Dr. de Schweinitz was widely known for his contributions to the science of ophthalmology, having devoted his research particularly to toxic amblyopias, the relation of autointoxication to ocular disorders, pathologic changes of various ocular diseases, relation of cerebral decompression to the cure of choked disk, ocular angiosclerosis, pathogenesis of choked disk, relation of focal infection to ocular diseases, blindness in Guernsey calves, comparative ophthalmology, ophthalmic surgery and pulsating exophthalmos. For this investigative work he achieved wide recognition. He was awarded the Leslie Dana Gold Medal in 1930 by the National Society for the Prevention of Blindness in cooperation with the St. Louis Society for the Blind. For this award he received the personal congratulations of President Herbert Hoover. He had also been called to attend Woodrow Wilson when he was President of the United States. The Howe prize medal in ophthalmology in 1927, the Huguenot Cross in 1928, the bronze plaque of the French Society for Ophthalmology in 1923, and the Alvarenga prize in 1894 were other honors to Dr. de Schweinitz.

The literary contributions of Dr. de Schweinitz included chiefly his textbook on "Diseases of the Eye," which has passed through numerous editions. Moreover, he participated in the editing and publication of seven additional textbooks in his field, and his original papers numbered hundreds.

Dr. de Schweinitz was conspicuous as a recognized leader in every activity in which he took part. He spoke with poetic and polished diction, always in behalf of the highest ideals of medical science. His manner was kindly and his presence was the personification of the dignity coupled with sincerity and humanity which are the characteristics of the truly great physician. His graciousness and nobility have been for many years a tradition among physicians.

John Martin Wheeler ✠ New York, professor of ophthalmology at the Columbia University College of Physicians and Surgeons, New York, died, August 22, at his summer home in Underhill Center, near Burlington, Vt., aged 58. Dr. Wheeler was born at Burlington, Vt., Nov. 10, 1879. He graduated from the University of Vermont in 1902, received the medical degree in 1905 and the master of science the following year. In 1928 Dr. Wheeler was appointed professor of ophthalmology at Columbia University and in 1931 director of the Institute of Ophthalmology of the Columbia-Presbyterian Medical Center. He was a member and past president of the American Academy of Ophthalmology and Oto-Laryngology, past president of the Society of Plastic and Reconstructive Surgery, a member of the American Ophthalmological Society and a fellow of the American College of Surgeons. Dr. Wheeler was consulting ophthalmologist to the Presbyterian, Fifth Avenue and Bellevue hospitals, Neurological Institute, Sloane Hospital for Women, and New York Eye and Ear Infirmary, New York, St. Luke's Hospital, Newburgh, N. Y., and Hackensack (N. J.) Hospital. He served during the World War as a captain and later as a major. In 1936 he was presented with the Leslie Dana Gold Medal for "outstanding achievements in the prevention of blindness and the conservation of vision" by the National Society for the Prevention of Blindness in cooperation with the St. Louis Society for the Blind. He was formerly a member of the board of directors of the National Society for the Prevention of Blindness. He was awarded the honorary degree of doctor of science by the University of Vermont in 1928 and by Middlebury (Vt.) College in 1933. Dr. Wheeler was also a member of the board of trustees of the University of Vermont. He achieved world wide fame as ophthalmic surgeon in many cases affecting notable people. His research was chiefly in the field of surgical technic applied to the eye and related structures.



JOHN M. WHEELER, M.D.
1879-1938

Howard Moore Williamson ✠ Lieut. Col., M. C., U. S. Army, Manila, P. I.; Washington University School of Medicine, St. Louis, 1915; fellow of the American College of Surgeons; served during the World War; entered the medical corps of the regular army as a first lieutenant in 1920, passing through the various grades to lieutenant colonel in April, 1938; aged 47; died, June 2, in the Sternberg General Hospital.

McLeod Gillies, Charleston, W. Va.; University of Manitoba Faculty of Medicine, Winnipeg, Manit., Canada, 1924; served during the World War; member of the West Virginia State Medical Association; on the staffs of the Mountain State, Kanawha Valley, St. Francis, McMillan and Staats hospitals; aged 45; died, June 21, in Baldur, Manit., of spontaneous pneumothorax of the right lung.

Walter Karl Seelye, Seattle; State University of Iowa College of Medicine, Iowa City, 1892; member of the Washington State Medical Association, American Academy of Ophthalmology and Oto-Laryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; aged 70; died, June 24, of arteriosclerosis and myocarditis.

William Edward Zilisch ✠ Wausau, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; past president of the Marathon County Medical Society; on the staffs of the Wausau Memorial Hospital and St. Mary's Hospital; aged 64; died, May 1, of Parkinson's disease.

Charles Garrard Daugherty, Paris, Ky.; University and Bellevue Hospital Medical College, New York, 1899; member of the Kentucky State Medical Association; past president of the Bourbon County Medical Society; aged 66; on the staffs of the Massie Memorial Hospital, where he died, June 8, of hypertensive heart disease.

George Foster Gourley, Steubenville, Ohio; Ohio Medical University, Columbus, 1903; member of the Ohio State Medical Association and the American Academy of Ophthalmology and Oto-Laryngology; on the staffs of the Gill Memorial Hospital and the Ohio Valley Hospital; aged 59; died, June 28, of coronary thrombosis.

Everett Nathaniel Bennett, Kokomo, Ind.; Western Reserve University School of Medicine, Cleveland, 1915; member of the Indiana State Medical Association; on the staffs of St. Joseph and Good Samaritan hospitals; served during the World War; aged 52; died, June 2, of chronic valvular heart disease.

George Joseph Youell, Philadelphia; Medico-Chirurgical College of Philadelphia, 1904; during the World War was chief medical examiner for a draft board; on the staffs of the Northeastern and St. Mary's hospitals; aged 55; died, May 30, in the Fitzgerald-Mercy Hospital, Darby, Pa., of cerebral hemorrhage.

George Oscar Switzer, Ludington, Mich.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1881; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; member of the Michigan State Medical Society; aged 84; died, June 15, in the Paulina Stearns Hospital.

John Robert Wilson ✠ Bennington, Vt.; Columbia University College of Physicians and Surgeons, New York, 1905; member of the American Academy of Ophthalmology and Oto-Laryngology; aged 58; on the staff of the Putnam Memorial Hospital, where he died, June 28, of acute myocarditis and nephritis.

John Nivison Force, Berkeley, Calif.; University of California Medical Department, San Francisco, 1901; chairman of the department of hygiene, University of California, and for many years professor of epidemiology; aged 60; died, June 21, in a hospital at San Francisco of carcinoma of the stomach.

Jesse Howard Robbins, Sioux City, Iowa; Sioux City College of Medicine, Sioux City, Iowa, 1895; member of the Iowa State Medical Society; formerly county coroner; on the staff of St. Vincent's Hospital; aged 67; died, June 18, of coronary thrombosis and arteriosclerosis.

James William Thomas, Cross Plains, Tenn.; University of Louisville (Ky.) Medical Department, 1910; member of the Tennessee State Medical Association; aged 60; died, June 21, in a hospital at Nashville of cerebral embolism and pulmonary embolus, following a cholecystectomy.

John Preston, Austin, Texas; University of Virginia Department of Medicine, Charlottesville, 1872; Bellevue Hospital Medical College, New York, 1873; formerly superintendent of the State Lunatic Asylum; aged 86; died, June 27, of acute cystitis and septicemia.

Gilce Dick Moore Lambdin, Electra, Texas; Kansas City Medical College, 1905; member of the State Medical Association of Texas; served during the World War; formerly health officer of Chautauqua County, Kan.; aged 54; died, June 25, of lymphosarcoma.

Chase Adam Shafer, Chester, W. Va.; Chicago College of Medicine and Surgery, 1917; past president of the Hancock County Medical Society; on the staff of the East Liverpool (Ohio) Hospital; aged 50; died, June 26, of carcinoma of the colon.

Robert Colwell Heflebower, Cincinnati; Miami Medical College, Cincinnati, 1889; fellow of the American College of Surgeons; aged 72; died, June 3, in the Good Samaritan Hospital of cerebral hemorrhage, following carcinoma of the prostate.

Lewis Henry Hector ✠ Long Beach, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1905; member of the Medical Society of the State of Pennsylvania; aged 59; died, June 24, of carcinoma of the cecum.

Thomas Sidney Whitelock Sr. ✠ San Diego, Calif.; Gross Medical College, Denver, 1899; aged 75; on the staffs of the Mercy Hospital and of the Scripps Memorial Hospital, where he died, May 25, of coronary occlusion.

William Cobb Whitfield, Salisbury, N. C.; University of Maryland School of Medicine, Baltimore, 1884; member of the Medical Society of the State of North Carolina; aged 77; died, May 13, of cerebral hemorrhage.

George L. Roark, Tabor, Iowa; Northwestern University Medical School, Chicago, 1918; member of the Iowa State Medical Society; aged 57; died, June 11, of chronic valvular disease and angina pectoris.

James Glover Tompkins, Edgefield, S. C.; University of the City of New York Medical Department, 1883; past president of the Edgefield County Medical Society; aged 85; died, June 12, of senility.

John Alfred Gillean, Dallas, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1885; aged 78; died, June 8, of coronary thrombosis, prostatic hyperplasia and arteriosclerosis.

Arlington Walton Diven, Martins Ferry, Ohio; University of the South Medical Department, Sewanee, Tenn., 1895; formerly county coroner; aged 66; died, June 4, of bronchopneumonia.

William H. Fuller, Friendship, Ind.; Cincinnati College of Medicine and Surgery, 1895; aged 66; died, June 6, in a hospital at Milan, of injuries received in an automobile accident.

Edward Russell Hanlon, Los Angeles; Cooper Medical College, San Francisco, 1899; member of the California Medical Association; aged 61; died, June 24, of chronic myocarditis.

Lawrence Edward Gausepohl, St. Louis; St. Louis College of Physicians and Surgeons, 1914; aged 50; died, July 5, of edema of the brain, chronic nephritis and chronic myocarditis.

Ira Albertum Tripp, Cleveland; Trinity Medical College, Toronto, Ont., Canada, 1895; aged 67; died, May 30, in a local hospital of pulmonary embolism and bronchopneumonia.

John Walton Smith, Payette, Idaho; University of Tennessee Medical Department, Nashville, 1894; member of the Idaho State Medical Association; aged 85; died, May 19.

James M. Hamilton, Oakmont, Pa.; Jefferson Medical College of Philadelphia, 1876; member of the Medical Society of the State of Pennsylvania; aged 88; died, May 20.

Edwardina M. Grant, Cleveland; Cleveland Homeopathic Medical College, 1902; aged 74; died, June 3, of carcinoma of the colon, arteriosclerosis and carcinomatosis.

Everett Field Darling, New York; Columbia University College of Physicians and Surgeons, New York, 1900; aged 63; died, May 9, in St. Luke's Hospital.

B. C. Maud Speer, Tamaqua, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1892; aged 73; died, May 24, in the Pottsville (Pa.) Hospital.

Bonnard Teegarden ✠ New York; Eclectic Medical College, Cincinnati, 1926; aged 35; died, June 28, in Tucson, Ariz., of coronary occlusion.

Adelard Odilon Falardeau, Fournier, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1921; aged 51; died, June 7.

D. Roy Hunt, Ellisville, Miss.; Memphis (Tenn.) Hospital Medical College, 1904; aged 68; died, in May.

John G. McClellan, Bristol, Tenn.; Eclectic Medical Institute, Cincinnati, 1889; aged 75; died, May 20.

Correspondence

PHYSIOLOGIC ACTION OF HYPOGLYCEMIA AND METRAZOL ON NERVOUS SYSTEM

To the Editor:—The investigations reported in THE JOURNAL, April 30, to which Favill refers in the issue of July 30, were on the physiologic action of hypoglycemia and metrazol on the central nervous system. They, together with a critical analysis of the physiologic mechanism involved in other therapeutic procedures successfully used in schizophrenia, led me to the theory that these procedures, introduced by the inventors for entirely different reasons, act by stimulating the sympathetic centers directly or indirectly. Clinical observations of Singer, the work of Hoskins and his collaborators, and that of others cited in the final paper (Gellhorn, Ernst: Effects of Hypoglycemia and Anoxia on the Central Nervous System, *Arch. Neurol. & Psychiat.* **40**:125 [July] 1938) support the conclusion that the sympathetic nervous system is deficient in these patients. The observations of Petersen that an aggravation in schizophrenic symptoms is accompanied by a fall of blood pressure is in line with the argument, although Petersen admits that similar changes of blood pressure frequently occur in normal persons. Moreover, the fall of blood pressure as such may be due to many different causes and is certainly not specific for a diminution in sympathetic tone.

The mechanism by which insulin evokes a sympathetic response is well established and referred to in any textbook of physiology.

I have not added a "new" proof that schizophrenic patients have a disturbance in the sympathetic centers. But the elucidation of the essential physiologic mechanisms by which the procedures commonly used in the treatment of this disease act created a new basis for therapeutic studies of this disease through animal experimentation, although the disease itself is not reproducible in them.

I believe with Cannon (The Pharos of Alpha Omega Alpha **1**, No. 2, 1938) "that value may follow from a polemic if the discussion is kept on a factual level."

ERNST GELLHORN, M.D., PH.D., Chicago.

BLOOD PRESERVATION TECHNIC

To the Editor:—In THE JOURNAL, July 23, appeared an article by Bernard Fantus describing the blood preservation technic used in the Cook County Hospital. I was surprised to see that with the technic described in this article the patient does not receive pure blood but blood diluted in equal parts with sodium chloride solution. When a blood transfusion is indicated, the patient ought to get the benefit of all the vital constituents of the blood in the physiologic concentration and not a highly diluted mixture. Such dilution is entirely unnecessary if one adheres to the original technic which I described nearly twenty-four years ago (A New and Greatly Simplified Method of Blood Transfusion, *M. Rec.* **87**:141 [Jan. 23] 1915).

I have repeatedly pointed out that unless the cannula is of proper size and is inserted properly into the vein, guaranteeing a rapid flow of the blood from the donor's vein into the glass receptacle, early stages of clotting will occur. When these few technical points are observed, dilution of the blood is absolutely unnecessary.

It is interesting to note that over twenty years ago the late Dr. Brem carried citrated blood to places seventy miles away from Los Angeles, the first practical application of the "stored blood" method. The storage of the blood originated in Russia. I think the Cook County Hospital was among the first institutions to popularize the method in this country.

While it is too early yet to pass definite judgment on the merits of the "stored blood" method, it would be unfortunate if the impression should be created that a dilution of the blood with equal parts of a sodium chloride solution was essential for the successful storage of blood. I am sure that many clinicians would object to using blood in this diluted form.

It is possible that storage of citrated blood may become very popular and be used extensively. For this reason it seemed of importance to point out that undiluted blood may be stored effectively.

Before closing I would like to suggest that the term "blood bank" which has been used for the storage of citrated blood be discarded. "Banks" are not only places of deposit but they are run for financial gain. As blood is stored in order to facilitate the technic and not for financial gain, "blood storage" or a similar term would be preferable.

RICHARD LEWISOHN, M.D., New York.

"DEFICIENCY OF VITAMIN B AND PEDICULOSIS"

To the Editor:—In THE JOURNAL July 16, page 257, is an editorial on "Deficiency of Vitamin B and Pediculosis." The author suggests that the corroboration of this fact would be helpful. I am interested in this remark, for on June 14, 1933, I read an article before the American Medical Association in Milwaukee: "Ocular Disturbances Produced in Experimental Animals by Dietary Changes." In this article I wrote: "At the end of ten weeks, animals on this diet were unable to care for their fur and their bodies were literally covered with lice."

ARTHUR M. YUDKIN, M.D., New Haven, Conn.

MEDICAL PORTRAITS ON STAMPS

To the Editor:—I was interested in the editorial in THE JOURNAL August 6 relative to medical portraits on stamps. I think too that we should have stamps for doctors of the United States. I am a collector of stamps relating to medicine. There has been one doctor in the United States that has been honored on a stamp, not so much because he was a good doctor but because he was a good diplomat and lawyer. Manasseh Cutler appeared on the Northwest Territory Stamp of this year. This will be found in "American History as Told by Postage Stamps," by Charles C. Gill, M.D., of Denver, and published by the *Weekly Philatelic Gossip* of Holton, Kan., page 28.

EVON WALKER, M.D., Ottumwa, Iowa.

EDITORIAL NOTE.—Manasseh Cutler was born in Killingly, Conn., in 1742, and graduated at Yale in 1765, according to the Encyclopedia Britannica. After being a school teacher and a merchant, and occasionally appearing in the courts as a lawyer, he decided to enter the ministry. From 1771 he was pastor of the Congregational church at what now is Hamilton, Mass. In the American Revolution he served as chaplain, thereafter supplementing his ministry by the practice of medicine and the conduct of a private boarding school. In 1786 he became interested in the settlement of Western lands, and in the following year, as agent of the Ohio Company, which he had taken a prominent part in organizing, he made a contract with Congress whereby his associates, former soldiers in the Revolutionary War and business men, might purchase 1,500,000 acres of land in the region north of the Ohio at the mouth of the Muskingum river. He also took a leading part in drafting the famous Ordinance of 1787 for the government of the Northwest Territory. From 1801 to 1805 he was a Federalist representative in Congress. A versatile man, Cutler conducted painstaking astronomical and meteorological investigations and made researches of scientific value in botany. He died in Hamilton, Mass., July 28, 1823.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DAY BLINDNESS OR NIGHT BLINDNESS

To the Editor:—In the article "The Pharmacology and Therapeutics of Vitamin A," by Dr. S. W. Clausen, it is said that night blindness "occurs in various diseases of the eye such as toxic amblyopia, retinitis pigmentosa and detachment of the retina." I have been taught that toxic amblyopia is a case of day blindess and not of night blindness. Who is right?

M.D., New York.

ANSWER.—Duke-Elder defines night blindness as the condition in which vision in moderate illumination is good but in feeble illumination is deficient. Day blindness is a symptom showing characteristics opposite to night blindness, the patient seeing poorly in good illumination and normally in the dusk. Central vision is a function of the fovea, which part of the retina has poor powers of dark adaptation. Consequently, disease (or congenital conditions) reducing the effectiveness of the peripheral portions of the retina throws the entire weight of vision on the fovea and there results the condition known as night blindness. On the other hand, in conditions in which the fovea does not function properly, as in toxic amblyopia, central vision, which is best under good illumination, is reduced and the burden of vision is thrown on the peripheral retina, which at best has a low visual acuity.

PHYSICAL THERAPY FOR DEEP TISSUES AND ARTHRITIS

To the Editor:—Which is preferable for the late treatment of injuries to the bones, muscles and ligaments—infra-red or short wave diathermy? In the use of the latter, is there any evidence to show deleterious consequence to delicate tissues, such as the eye or brain, in treating, for example, the sinuses? Which is preferable for the treatment of the pain from arthritis? It seems impossible to get anything but a "Scotch verdict" from the textbooks, and I am suspicious of the claims made by the manufacturers.

CLEMENT H. ARNOLD, M.D., Palo Alto, Calif.

ANSWER.—Any answers to these questions must be of a qualifying nature owing to the great multitude of factors influencing the end results of treatment. Such factors include (1) the individual reaction (idiosyncrasies of the patient), (2) the area to be treated and (3) the dosage.

While all three of these must be considered, it is the third which offers the chief difficulty in physical therapy. The dose depends almost entirely on the method of administration; different technicians differ both in technic and in judgment. X-ray therapy, in which the dosage can be quite accurately controlled, is a striking exception. In short wave diathermy, for example, the dose and the result will in part depend on the amount of current used, the size of and the distance between the electrodes and the spacing between the electrodes; i. e., the distance from the skin and, of course, the time or duration of the treatment. In the case of infra-red radiation, the dosage would depend in part on the power of the lamp, the distance from the lamp to the skin, the anatomic structure and depth of the part treated, and the duration.

In the treatment of bones, muscles and ligaments, the choice between infra-red radiation or short wave diathermy should perhaps be made on the accessibility of the part to be treated. In case the injury is comparatively superficial, infra-red may well be chosen. It is perhaps more economical, easier to manipulate, and above all easier to control and thus less dangerous. Furthermore, the part treated is more easily inspected and may, if desired, be subjected to brief intermittent massage applications during the administration of heat. The effectiveness of the treatment may also be varied by the application of counterirritants, or by wet compresses. The latter may be kept on continuously during the treatment if moist heat is desired. The compress is kept hot by the lamp, and more water is periodically poured on the cloth to replace that which evaporates. This is an effective method, for example, of keeping a continuous hot boric acid compress on open wounds.

A second and equally important, if not more important, question is How much heat should be introduced? Little or no work has been done on this all important problem. The tendency among those interested in physical therapy seems to be to concentrate on means to create higher temperatures and then to evaluate the efficiency of an apparatus on this basis. This is to be regretted, since there appears to be no information available which indicates that it is better to treat a sprained ankle by a temperature of 106 F. than, for example, 102 or 103.

The matter of dosage (temperature and time) is also an open question. The present tendency is, it appears, to treat to the patients' tolerance, but no data which tend to support the theory that such intense doses are more desirable than some lesser ones are available.

There should be no deleterious consequences to delicate tissue, such as the eye or brain, in treating, for example, sinuses by short wave diathermy, provided the dose is kept within safe limits.

There appears to be no generally accepted physical treatment for the pain of arthritis. This is due, no doubt, to the many forms of arthritis and the difficulty of correct diagnosis.

While at present the effects of short wave diathermy are attributed solely to the heat produced, there are present, no doubt, other secondary effects from the current—effects which have not as yet been segregated satisfactorily but which, if once isolated, may prove of therapeutic significance.

HAIRY BLACK TONGUE

To the Editor:—A man about 30 years of age has hairy black tongue. The case is typical and microscopic study presents numerous broken streptothrix filaments in the field. The condition is of about seven weeks' standing and is gradually becoming worse. The Wassermann reaction is negative. Oral hygiene has been carried out as well as abstinence from tobacco and also hot and acid foods. I have searched as much literature as I have at my disposal and can find no definite treatment for this condition. I would appreciate any suggestions in the way of therapy and prognosis.

CHARLES F. ENGELKING, M.D., Dalton, Ga.

ANSWER.—Hairy black tongue (nigrities, hyperkeratosis) is a hypertrophy of the filiform papillae of all or a portion of the medial dorsum. It usually comes on insidiously and without demonstrable cause, is asymptomatic and unimportant clinically, may remain for weeks or years, and is resistant to treatment. The failure of normal exfoliation of cellular scales results in the harboring of great numbers of bacteria in the abnormal papillary tufts. These bacteria may be staphylococci, streptococci, yeast, spore formers or Leptothrix, but when a Penicillium such as Mucor niger is present the color may be black. It is believed that this is coincidental to the coating.

Other causes of the hyperkeratosis include the use of oxidizing agents (such as sodium perborate), the presence of a hyperacidity or of a gastritis with or without hyperacidity (including neoplasm), irritating mouth washes or fever. Other possible causes of the dark coloration include silver nitrate, tannic acid, ferric chloride in the presence of blood, and dark coloring matter in medication or food.

There is no relationship between black tongue of man and that of dogs (which is caused by a vitamin deficiency).

The literature suggests the use of scrapers and salicylates to rid the tongue of the excess tissue but indicates that this is not remarkably effective.

Since the present case is not responsive to hygienic measures and is apparently complicated by the presence of a streptothrix, it is suggested that local applications of thymol or its isomer carvacrol be used. Thymol is effective against molds, is only slightly soluble in water, and is highly effective as a mouth wash in saturated solution (1:1,000).

COLD AND HOT COMPRESSES IN CELLULITIS

To the Editor:—What is the rationale of cold compresses of magnesium sulfate in cellulitis?

ROBERT A. ROBINSON, D.D.S., Albany, N. Y.

ANSWER.—Hot wet dressings produce an edema of the underlying tissues and capillary changes in the vessels with a varying amount of cellular infiltration. This may either hasten resolution or aid localization of the infection. Wet dressings are contraindicated when the tissues will not permit increased swelling without danger of spreading the infection and producing deeper involvement of tissues, cavities or fascial spaces. Under these conditions, before drainage is indicated cold compresses are desirable since they tend to lessen the congestion and also tend to relieve the pain. It is not desirable to apply constant ice cold compresses owing to danger of ischemia with lowered resistance of the tissues and also because relief of pain may delay necessary drainage.

There is often relief of pain by the cold produced by the evaporation of solutions if the dressings are not too thick. For

this purpose a 60 per cent alcohol solution or equal parts of boric acid solution and alcohol may be applied at frequent intervals.

A 25 per cent solution of magnesium sulfate probably has no advantage over boric acid solution or water, although it has an anesthetic action, but like lotion of lead and opium it is not absorbed to any appreciable extent through the unbroken skin. After incision of a suppurating area the use of a 25 per cent solution of magnesium sulfate favors relief of pain, a decrease of swelling and the separation of the necrotic tissue.

The protective and splinting action of dressings and the soothing reaction which follows the application of a cool or easily evaporating solution is often credited to the analgesic effect of some popular lotion. In acute inflammation, where increased swelling will not tend to spread the infection, and in the chronic or subacute forms hot wet dressings are usually indicated.

CUPPING OF NAILS IN INFANT

To the Editor:—I have under observation a boy baby aged 9 months. He is apparently normal in every way except for a slight cupping of his finger nails. There is a slight concavity on the exposed surface of the nails, especially pronounced on the index and middle fingers of both hands. The toe nails are slightly concave also. This nail change has become apparent only in the last two months. When the child was 3 months old he had a temperature of the type seen in tertiary malaria, reaching as high as 103.5 F. with a leukopenia of 4,000. Hemoglobin was 70 per cent. No plasmodia of malaria were found. The baby was placed on quinine sulfate and tincture of ferric chloride and within one week he was fever free. He has shown a normal weight gain throughout his life. His diet consists of pasteurized milk, Karo, egg yolk, pablum, vegetables and cod liver oil. What dietary change might be made and what mineral or vitamin therapy would be indicated? There is no dermatologist in this vicinity.

M.D., Illinois.

ANSWER.—The condition described is suggestive of several conditions affecting the nails. The first possibility is a rare condition of unknown etiology known as koilonychia, or spoon nails. This is a progressive condition usually beginning in one or more fingers and extending into the others. The other possibility which must be considered is that of a postinfectious dystrophy of the nails, or onychatrophy. This condition infrequently follows a severe systemic infection or infectious disease and may be characterized by crumbling, spotting or fragility of the nails. The lapse of four months before the appearance of the cupping does not rule this out as the etiologic factor. The child apparently had a systemic disease probably grippal in character.

The treatment of this condition consists in building up the general health of the child. No mention was made of vitamin C in the diet described and if this has not been administered it should be started at once in the form of orange or tomato juice. An iron tonic should be added.

Other cereals, vegetables and liver soup, mashed ripe banana, apple sauce and baked potato should also be added gradually to the diet at this age.

The local treatment of this condition is unsatisfactory. If there is no fragility or crumbling of the nail substance, nothing needs to be done. If there should be splitting or breaking, the hands should be protected by stocking or celluloid cuffs.

TELANGIECTASIA AND NASAL HEMORRHAGES

To the Editor:—A man, aged 63, has hereditary familial telangiectasia. He has had profuse hemorrhages from the nose since the age of 20. The nasal mucous membrane shows miliary telangiectatic spots as well as extensive ulcerations extending into the depths of the nose. In the past he has tried methods of increasing the coagulability of the blood such as thromboplastin, alum and snake venom. He has also used local measures, such as ice and nasal pressure. Small transfusions of from 200 to 300 cc. have erased the bleeding for several days. In spite of all these measures he still bleeds profusely and has an anemia with a hemoglobin of approximately 45 per cent. I would appreciate any help that you will offer.

BERNARD SELIGMAN, M.D., Brooklyn.

ANSWER.—As a rule, telangiectasia affects the vessels of the nasal septum in its cartilaginous portion and in the vast majority of cases these vessels can be destroyed by the galvanocautery. In elderly persons hypertension may be the predisposing cause of recurring hemorrhages from the septum, middle turbinate and even the antrum.

Since the usual local measures have failed and, in addition, various constitutional agents have been given without avail, it would be advisable to try radium, which may cause sufficient fibrosis to contract the offending vessels or even cause them to disappear. A capsule containing 25 mg. of radium element sheathed in thin rubber tubing is inserted into each nasal cavity at about the level of the lower border of the middle turbinate, being kept in place by gauze packing below as well as above. The radium is left in place for four hours, making a total of 200 mg. hours administered. This dose may be repeated within two weeks without danger. The ulcers will undoubtedly heal but one will have to expect a certain amount of atrophy to take place as a result of the irradiation. It will be necessary, therefore, to keep the nasal cavities well lubricated with petrolatum or liquid petrolatum for an indefinite period. The patient should also be warned of the possibility of anosmia resulting from the atrophic changes in the mucous membrane.

HYPNOTICS

To the Editor:—Please discuss the use of hypnotic drugs not belonging to the barbituric acid or bromide groups to which there is frequent objection. What drugs would you advise for topical application to the sigmoid or rectum in ulcerated colitis?

M.D., Washington.

ANSWER.—There is probably no hypnotic that is entirely without disadvantage, but one of the least objectionable is carbromal (a 0.3 Gm. tablet at bedtime), which is essentially not a bromide. It may give rise to acne in persons highly susceptible to bromide. Chloral hydrate is an old reliable remedy; in a dose of 1 Gm. taken freely diluted in milk, it will compel sleep; like all other powerful hypnotics, it is habit producing and therefore should be prescribed with the necessary precaution against habituation. One such measure is to prescribe the chloral in syrup of glycyrrhiza (1 Gm. to 5 cc.) in a 100 cc. bottle, to have the patient add a teaspoonful of water for each teaspoonful of medicine he has taken. It is also well to have the patient take a dose only on those nights when he is unable to sleep and has not slept well for a night or two before. The use of all such hypnotics must be accompanied by treatment directed against the cause of the insomnia.

The kind of topical application to be used in ulcerative colitis depends on the acuteness of the condition. Only soothing applications are tolerated in the acute form and among these might be mentioned bismuth subgallate, 1 tablespoonful to 500 cc. of starch water, to be retained as long as possible and given once daily after a cleansing enema.

PROBABLE MENINGOVASCULAR SYPHILIS

To the Editor:—A Negro aged 27, whom I had the opportunity of seeing only once, had recurrent headaches for the past three months, increasingly severe, the attacks beginning in the right frontal region and spreading across the forehead, over the entire head and down the back of the neck. There is no nausea or vomiting. There have been transitory diplopia, attacks of vertigo with syncope, periodic swelling of both orbital regions, usually greater on the right, and two or three attacks of partial blindness in the right eye, no visual defects having been noted in the left eye. He has had no edema of other parts of the body or face. His past history is negative for syphilis, but a Wassermann test of the blood, taken a few weeks ago on account of persistent headache, was 4 plus. The patient has refused lumbar puncture. Urinalysis has not been done. The pulse rate is 50 and the blood pressure 150 systolic, 100 diastolic. The pulse is strong and full. The patient is in great pain but well oriented. His speech is normal. His neck is slightly stiff. The right pupil is fixed in mid-dilatation and is regular. There is a small retinal hemorrhage lateral to the disk but no papilledema. The left pupil was regular and reacted briskly to light; the left fundus was not observed satisfactorily. There was no evidence of other cranial nerve injury. Vision was not tested. General physical examination was negative. The most probable diagnosis here, I think, is acute meningovascular syphilis. But in the presence of symptoms predominant on the right side and of unilateral (right eye) abnormalities should not intracranial neoplasm also be suspected? How often does a unilateral Argyll Robertson pupil occur?

M.D., Oklahoma.

ANSWER.—The unilateral fixed and partially dilated pupil conforms to that seen in meningovascular syphilis. The pupil as described is not an Argyll Robertson pupil. The Argyll Robertson pupil in its narrow sense is a contracted pupil. The Argyll Robertson pupil is at times unilateral. The syphilitic pupil, corresponding to the one described, is frequently unilateral. This is referable to a lesion of the third cranial nerve. The transient attacks of diplopia may have the same basis.

In the case cited the observations given warrant the diagnosis of meningovascular syphilis. The examination of the spinal fluid would, however, be necessary to confirm the diagnosis. In the event that the spinal fluid showed no evidences of syphilis, the diagnosis of an expanding intracranial lesion would be favored. It is evident that the short duration and the progressive nature of the symptoms indicate an acute process. The spinal fluid should be strongly positive if the diagnosis of syphilis is correct. In face of the patient's refusal to have a spinal puncture, the therapeutic test with antisyphilitic treatment may be substituted and should give rapid improvement if the diagnosis is correct.

NEUROSYPHILIS AND DERMATITIS FROM ARSENICALS

To the Editor:—A woman aged 29 complained of ataxia and dizziness in July 1937. She had a vertical and lateral nystagmus, sluggishly reacting pupils, hyperactive tendon reflexes and a slight Romberg sign. The Wassermann reaction was strongly positive. She was unaware of her infection and I could not determine the date of onset. A dose of 0.25 Gm. of neoarsphenamine intravenously produced an extensive exfoliative dermatitis which took about three weeks to improve with local treatment and sodium thiosulfate. There was also considerable temporary loss of hair from the scalp. She was then put on 0.2 Gm. of thiobismol in 2 cc. of water intramuscularly twice weekly. She also received iodides to tolerance. She has had forty treatments to date and is greatly improved, but the Wassermann reaction is unchanged. Her mouth is almost endentulous and she wears dentures, but there is a tendency to stomatitis if treatment is pushed. I have not examined her spinal fluid yet, as it is probably positive and I can make little change in treatment anyway. I do not feel that I am warranted to try the arsenicals again. Could you suggest further treatment? Should I try mercury, mapharsen, tryparsamide, sulfarsphenamine or acetarsone? Are the oily bismuth preparations superior to the water-soluble ones?

M.D., Oregon.

ANSWER.—This patient cannot be treated intelligently without examination of the spinal fluid and without accurate neurologic and psychiatric definition of the type of neurosyphilis from which she suffers. The information given is inadequate for this purpose. If there is any serologic or psychiatric indication that she is suffering from dementia paralytica, she should immediately be treated with artificial fever, preferably by induced malaria.

Whatever type of neurosyphilis she may have, and whether fever is indicated, her treatment should certainly include the use of tryparsamide. This pentavalent arsenical drug may be safely given to patients sensitized against the arsphenamines.

No effort should be made to give the patient mapharsen, sulfarsphenamine or any other trivalent arsenical, since another attack of dermatitis will almost surely be precipitated. Acetarsone is wholly in the experimental stage in the treatment of syphilis and should not be used.

Compounds of either of the heavy metals mercury or bismuth alone, or in combination with each other, are inadequate to control neurosyphilis.

Current information as to the relative value of water soluble, oil soluble and insoluble oil suspensions of bismuth indicates that they are of approximately equal value, provided treatment is used specifically to take into account the factors of absorption and excretion. The water soluble products are absorbed and excreted so rapidly that treatment should be given either daily or every other day; the oil soluble products occupy an intermediate position and should be given twice a week; the insoluble oil suspensions are absorbed and excreted most slowly and may be given once a week.

INSULIN FOR DIABETIC PATIENT IN CORONARY DISEASE AND PNEUMONIA—HIGH PLASMA CHOLESTEROL

To the Editor:—A woman, aged 60, affected by mild diabetes with fasting blood sugar 185, is on a restricted carbohydrate diet. On account of her heart condition—incipient sclerosis of the coronary arteries—it has been decided not to give insulin because of its damaging effects in these conditions. Recently she fell sick with influenza and bronchopneumonia and the problem was whether dietary rules such as the carbohydrate restriction should be disregarded during the acute illness. What can be done to lower the cholesterol content in the blood of this patient?

M.D., New York.

ANSWER.—Three questions are raised in this case:

1. Should the patient receive insulin? The inquirer does not say just what is meant by "incipient sclerosis of the coronary arteries." Insulin itself is not contraindicated in coronary sclerosis, although insulin reactions are dangerous. If a patient needs insulin he should receive it, but it is well to be particularly careful to keep the dose below the point at which insulin reactions may occur. If there is not much sugar in the urine, no great concern need be attached to a value of 185 mg. of sugar per hundred cubic centimeters of blood; but, if sugar is present in the urine, the patient should receive sufficient insulin to control the amount of sugar in the urine, particularly in the first specimen passed on arising.

2. How much attention should be paid to the diabetic diet during the period of an associated illness? This question arises not only in cases of infection of the upper part of the respiratory tract, as in this case, but also in such conditions as peptic ulcer and chronic ulcerative colitis. In general, it is possible to control diabetes with almost any type of diet that is necessary, and in those cases in which the diet for an associated condition is of more importance to the patient's health than the diet for diabetes the dietary regimen for diabetes should be disregarded and the diabetes should be controlled with the changed regimen. In primers for diabetic patients, such as those written by Joslin and by Wilder, there are excellent suggestions for temporary dietary changes in cases of associated complicating illness.

3. What can be done to lower the concentration of cholesterol in the plasma? The concentration of cholesterol in this case is not stated. The relationship of plasma cholesterol and other plasma lipoids to diet has not yet been finally answered. There is strong experimental evidence that the concentration of lipoids in the plasma is definitely related to the amount of fat ingested, but almost all the studies have been made on animals, which ordinarily do not eat any fatty foods. Therefore it has been virtually impossible to reproduce these results in animals which eat a general diet such as is eaten by man. The belief in the importance of a high carbohydrate, low fat diet is subscribed to by many but is not accepted by other equally capable men; however, until this problem is settled, it probably is best to restrict the amount of fat in the diet in cases in which the concentration of lipoids in the plasma is high.

INK AS CAUSE OF NEURITIS?

To the Editor:—A man aged 20, a printer for four years, uses news black and job ink, every day, made by the International Printers' Ink Corporation. Is there anything in this ink that could cause neuritis? All known tests for the cause of neuritis have been made and are negative.

ONAL A. SALE, M.D., Neosho, Mo.

ANSWER.—Nothing in the types of inks mentioned is known to be a source of neuritis as the sole manifestation of injurious action. In some operations connected with printing, highly repetitive, stereotyped motion conceivably might lead to a neuritis. Likewise, some chemicals that might be used, such as type cleaning fluids, might provoke a neuritis on rare occasions. At times the drying fluid used in connection with offset printing may lead to sensitization and a neuritis is not entirely impossible.

PROBABLE DERMOID CYST OF NOSE

To the Editor:—A girl aged 3½ had at birth a small cyst on the middle of the bridge of the nose. This cyst contained a small amount of white, rather sebaceous, material when opened. It has not refilled and is represented at present only by a small pit or porelike depression in the skin in the bridge of the nose. What would be the best treatment for this small lesion?

PHILIP T. HOLLAND, M.D., Bloomington, Ind.

ANSWER.—A cyst or cystlike lesion in the midline anywhere appearing at birth speaks for a developmental anomaly, most probably a dermoid cyst. At the midline of the nose it is not likely to be a branchial or thyroglossal cyst. Sebaceous cysts are not likely to occur at birth, though of course they are by no means impossible then.

It would be the conservative procedure to let this healed lesion alone, even though the present healing may be only temporary. If there should be a reactivation with refilling of the cyst, it would then be time enough to take action. The extent of the cyst wall would indicate itself better then and appropriate measures would secure its elimination.

MISSED ABORTION

To the Editor:—A young married woman last October had a rather heavy period. Thereafter she missed some periods and had others scantier and shorter than normal; she had morning nausea, enlargement of the breasts and abdomen, and a gain in weight. The gain corresponded to a normal pregnancy until January; it then remained stationary for two months and then she lost 4 pounds (1.8 Kg.). From October on she had no leukorrhea, fever or chills and felt well except for backache. Early in April she had cramps and flowed heavily for three days, and the physician who examined her said she needed a curettage because of the placental tissue of a miscarriage of October had remained and that a retroverted uterus would not have permitted her to be pregnant for any long period. Please comment on this, especially as to the possibility of the placenta remaining that long without causing trouble.

M.D., Iowa.

ANSWER.—It is difficult to make a diagnosis from the information given. The patient could have been pregnant, the embryo dying after several months' development and the expulsion failing to take place. In the so-called missed abortions all the symptoms and signs of early pregnancy are present but disappear. The uterus becomes progressively smaller. The products of conception may remain in the uterine cavity for many months without producing symptoms. As a rule, no bleeding occurs during this time. Bleeding may begin when the uterine cavity begins to evacuate its contents.

It is likewise possible that the patient was not pregnant at any time but that the amenorrhea of several months was the result of an endocrine disturbance. Sometimes a corpus luteum cyst causes a period of amenorrhea.

It is possible for a patient to continue with a normal pregnancy in a retroverted uterus. Usually the position of the uterus is corrected before the third month of gestation when the organ ceases to be confined to the pelvis but rises above the brim into the abdomen. Only rarely does abortion occur as a result of a retrodisplacement.

If the uterus is normal in size and normal menstrual periods have returned, dilation and curettage are not indicated. On the other hand, if the patient has irregular periods of bleeding it may be well to perform this minor procedure.

INCUBATOR HUMIDITY

To the Editor:—Is the degree of humidity in the incubator for premature infants considered to be of much importance? If so, what is considered to be the proper humidity? CARL IRENEUS, M.D., Chicago.

ANSWER.—The degree of humidity in an incubator must, of necessity, vary, first with the size of the infant, second with the temperature of the infant, third with the temperature at which the bed is heated and fourth with the exchange of air within the bed itself. In practical experience a relative humidity varying between 40 and 50 degrees within the bed is desirable. It should be remembered that with higher temperatures the relative humidity should be lower than with a lower temperature atmosphere. A large infant furnishes more heat in a closed bed than does a small premature infant, and a patient with a high temperature and increased respiration gives off more moisture than one with normal temperature. A rapid exchange of air in the bed also tends to keep the humidity at a level more nearly that of the surrounding room temperature. With a free current of air passing in and out of the bed there is little need for concern as to the child's welfare unless the surrounding air is especially dry.

HYPERTROPHY OF HAIR AFTER PLASTER CAST

To the Editor:—What is the explanation given for hypertrophy of hair found on removal of plaster casts? M.D., New York.

ANSWER.—Others corroborate this observation. No controlled studies have been found bearing on the question. This leaves the explanation open to conjecture.

STERILIZATION OF COCAINE HYDROCHLORIDE SOLUTIONS

To the Editor:—In THE JOURNAL July 16 a query appears under the heading "Sterilization of Cocaine Hydrochloride Solutions." In 1886 I began using cocaine solution chiefly in surgical practice, but later on in eye operations. Learning almost at once that the solution was unstable and deteriorated rapidly, I did a lot of experimenting and found that the addition of three drops of carbolic acid to a solution of cocaine hydrochloride (of any given amount) in an ounce of distilled water not only kept it absolutely sterile but prevented decomposition and loss of anesthetic power. I used control experiments and found not the slightest change at the end of a year. I have used it extensively in eye enucleations, strabismus operations and various other operations on the eye with the most satisfactory results and entire freedom from infection. The only drawback is that the first instillation causes a little more smarting than when it is made with distilled water. Subsequent instillations are not felt. It forms a precipitate, however, with the procaine hydrochloride-sodium chloride solution of Labat and others. If the inquirer desires further information on the subject or on the preparation of homatropine, physostigmine (eserine) and the like used in eye treatments, he may be referred to the final paragraph on page 198 and to page 212 of my "Fifty Years a Country Doctor" (New York, E. P. Dutton & Co.), which was recently reviewed in THE JOURNAL. Information regarding the preservation of cocaine solutions is given there.

WILLIAM N. MACARTNEY, M.D., Fort Covington, N. Y.

STERILIZATION OF RUBBER GOODS

To the Editor:—Under the caption "Sterilization of Rubber Boots and Shoes" in THE JOURNAL, July 2, page 81, Dr. George M. Blank of Lorain, Ohio, asks for "the simplest and most effective method of sterilizing rubber boots." While I have not had occasion to sterilize rubber boots I do have occasion to use many times daily rubber apron finger cots for rectal, vaginal and other forms of physical examination. Formerly I had great difficulty in ascertaining how to sterilize as well as preserve them. About ten years ago I began to wash these rubber finger cots with running water and a hand hairbrush, and then in soap and water, and again in clear running water to wash off all the soap, and then keep them immersed in a small basin of 1:2,000 aqueous solution of mercury bichloride. This cleans and disinfects them, and the mercury solution apparently preserves the rubber so that instead of being thrown away after each use they can be used over and over again many times before showing evidence of deterioration. It is suggested that this be tried with other rubber goods and the results reported. PAUL R. STALNAKER, M.D., Houston, Texas.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ALASKA: Juneau, Sept. 6. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science.* Tucson, Sept. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Medical (Regular).* Little Rock, Nov. 3-4. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic).* Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock. *Basic Science.* Little Rock, Nov. 7. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock.

CALIFORNIA: *Reciprocity.* San Francisco, Sept. 14, and Los Angeles, Nov. 16. *Written examination.* Sacramento, Oct. 17-20. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Oct. 5-7. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Oct. 8. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Regular).* Hartford, Nov. 8-9. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homeopathic).* Derby, Nov. 8-9. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Dec. 26-27. *Medical.* Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 14-15. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 11-12. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Oct. 4-5. Commissioner of Law Enforcement, Hon. J. L. Balderston, 205 State House, Boise.

ILLINOIS: Chicago, Oct. 18-20. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Oct. 11. Corres. Sec., Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KENTUCKY: Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 8-9. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical (Regular).* Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic).* Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 8-10. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: Lansing, Oct. 12-14. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Oct. 4-5. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Oct. 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: Kansas City, Oct. 18-20. State Health Commissioner, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

MONTANA: Helena, Oct. 4. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Lincoln, Oct. 4-5. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 7-9. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, Sept. 15-16. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW JERSEY: Trenton, Oct. 18-19. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 10-11. Sec., Dr. Le Grand Ward, 135 Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, Sept. 19-22. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity.* December. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical.* Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Basic Science.* Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: Santurce, Sept. 6-10. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

RHODE ISLAND: Providence, Oct. 6-7. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, Nov. 8. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Bluefield, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: *Basic Science.* Madison, Sept. 24. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical.* Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Oct. 3 (probable date). Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the *National Board of Medical Examiners* and *Special Boards* were published in THE JOURNAL, August 27, page 867.

Alabama June Examination

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports the examination held at Montgomery, June 28-30, 1938. The examination covered ten subjects and included 100 questions. Twenty-nine candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Emory University School of Medicine		(1936)	83.4, (1938) 79.5, 88, 89.4, 89.9
University of Georgia School of Medicine		(1938)	86.5
Northwestern University Medical School		(1938)	90.7
Rush Medical College		(1937) 88.5, (1938)	85.7
School of Medicine of the Division of Biological Sciences		(1937)	92.2
Tulane University of Louisiana School of Medicine		(1938)	82.5, 84.6, 86.7, 87.3, 88, 90.9
Harvard University Medical School		(1934) 89, (1937)	92.5
Washington University School of Medicine		(1938) 85.4,	90.3
Cornell University Medical College		(1938) 87.5,	90.6
University of Oklahoma School of Medicine		(1937)	84.9
Jefferson Medical College of Philadelphia		(1937)	89.6
University of Pennsylvania School of Medicine		(1936)	89.2
University of Tennessee College of Medicine		(1937)	76.3
Vanderbilt University School of Medicine		(1938)	88
Dalhousie University Faculty of Medicine		(1937)	81.8
University of Western Ontario Medical School		(1933)	90.3

Fifteen physicians were licensed by reciprocity from May 9 through July 27. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Howard University College of Medicine		(1935)	Kansas
Northwestern University Medical School		(1934)	Ohio
University of Louisville School of Medicine		(1937)	Kentucky
Tulane University of Louisiana School of Medicine		(1934), (1935), (1936), (1937)	Louisiana
Detroit College of Medicine and Surgery		(1919)	Michigan
University of Michigan Medical School		(1927)	Michigan
St. Louis University School of Medicine		(1935)	Missouri
Washington University School of Medicine		(1936)	Missouri
Medical College of the State of South Carolina		(1937)	S. Carolina
Vanderbilt University School of Medicine		(1932), (1935)	Tennessee
Medical College of Virginia		(1920)	Virginia

Mississippi June Report

Dr. Felix J. Underwood, executive officer, Mississippi State Board of Health, reports the written examination held at Jackson, June 22-23, 1938. The examination covered twelve subjects and included ninety-six questions. An average of 75 per cent was required to pass. Thirty-two candidates were examined, thirty-one of whom passed and one failed. Sixteen physicians were licensed by reciprocity and one physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine		(1938)	84.3
Emory University School of Medicine		(1938)	87.9
Northwestern University Medical School		(1938)	90.1*
University of Louisville School of Medicine		(1938)	90.7
Tulane University of Louisiana School of Medicine		(1937)	84.6, 88.4, (1938) 84.8, 87.4, 87.6, 87.9, 88.5
University of Tennessee College of Medicine		(1935)	83.2, (1937) 80, 80.1, 81, 82.7, 85.3, 85.7, 87.6, (1938) 81.7, 82, 82.4, 83.1, 84.8, 85.4, 86.2, 89.7
Vanderbilt University School of Medicine		(1938)	84.7, 84.8, 85.8, 87.3

	FAILED	Per Cent
Nongraduate		60.5†

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1936)	Arkansas
Jenner Medical College, Chicago		(1902)	Texas
Tulane University of Louisiana School of Medicine		(1922) (1936)	Penna., Louisiana
University of Michigan Medical School		(1936)	Michigan
Creighton University School of Medicine		(1925)	Nebraska
Ohio State University College of Medicine		(1922), (1936)	Ohio
University of Cincinnati College of Medicine		(1917)	Ohio
University of Pittsburgh School of Medicine		(1931)	Penna.
Memphis Hospital Medical College		(1903)	Tennessee
University of Tennessee College of Medicine		(1928), (1933), (1937, 3)	Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Vanderbilt University School of Medicine		(1936)	N. B. M. Ex.

* This applicant has received the M.B. degree and will receive the M.D. degree on completion of internship. License has not been issued.
† Permitted to take the examination by special act of the legislature.

Book Notices

The Foundations of Nutrition. By Mary Swartz Rose, Ph.D., Professor of Nutrition, Teachers College, Columbia University. Third edition. Cloth. Price, $3.50. Pp. 625, with 116 illustrations. New York: Macmillan Company, 1938.

The last edition of this popular textbook was published five years ago. The author now has brought the material to date, while retaining all the charm and readability for which the earlier editions have been noted. A feature of the book is the historical treatment accorded each section. This material is written in a style which leaves the reader with a feeling that, in some way, he has been permitted a peek into the laboratories and clinics where classic researches have been developed. The book covers the entire field of nutrition. As an example of the thorough method of presenting a subject, the chapter on vitamin G can be regarded as more or less typical. In this chapter there are discussions of the discovery of vitamin G and the isolation of riboflavin, the importance of this factor in the promotion of growth and the maintenance of the health of the skin and eyes and the prevention of experimental cataract, the probable value of riboflavin in the maintenance of health and vigor of all ages and, finally, discussions of methods of measurement, food sources and requirements. The illustrations for this particular chapter include photographs of a chicken fed on a normal ration and another fed on a G-deficient diet, several charts of growth curves of rats fed on diets lacking in vitamin G, a good illustration of crystals of riboflavin, several pictures of rats showing signs of vitamin G deficiency, a curve showing the resumption of growth after a vitamin G-free diet in the rat, a picture of a turkey fed on a vitamin G-deficient diet, and showing eyelids stuck together and incrustation of the mouth and nostrils, a picture of cataract in rats, and an illustration of sixteen common foods in dishes, each food being represented by the portion that would supply approximately 50 units of vitamin G. There is a selected list of references at the end of the chapter. The same thorough treatment is given each topic. The book is copiously illustrated with well chosen charts, diagrams and reproductions of photographs. There are extensive tables of food values and other useful tables in the appendix. The book should be in the library of every person interested in foods and nutrition.

Studies on Biological Oxidation and Some of Its Catalysts (C4 Dicarboxylic Acids, Vitamin C and P etc.). By Albert v. Szent-Györgyi, M.D., Ph.D., Professor of Medical and Organic Chemistry, University of Szeged. Acta Litterarum ac Scientiarum Reg. Universitatis Hung. Francisco-Iosephinae, Sectio Medicorum. Tome IX, Fasc. 1. Redigunt: J. Baló, D. Miskolczy et St. Rusbnyák. Paper. Price, 5 marks. Pp. 98, with 12 illustrations. Leipzig: Johann Ambrosius Barth; Budapest: Eggenbergersche Buchhandlung Karl Rényi, 1937.

To many persons it may have been a matter of surprise that Szent-Györgyi was awarded a Nobel prize in 1937 chiefly for his work on biologic oxidations rather than for his better known work on the isolation of vitamin C. This little volume explains how the isolation of vitamin C was, in a sense, a by-product of investigations of the as yet incompletely understood mechanism of the oxidation of foodstuffs in tissues. Szent-Györgyi, who had discovered in animal tissues the catalytic nature of those dicarboxylic acids which contain four carbon atoms, investigated also oxidation systems in plant tissues. A substance having marked reducing properties was isolated from both plant (citrus fruit juices, cabbage leaves) and animal tissue (adrenal glands). This fundamental, widely distributed reducing agent of cells, either of animals or of plants, first was called hexuronic acid. Its antiscorbutic properties were not discovered until several years later. "From the very beginning," writes Szent-Györgyi, "I suspected ascorbic acid to be identical with vitamin C but my roaming life was unsuited for vitamin tests and moreover, somehow or other, vitamins were my pet aversion. Vitamins owe their great popularity to their paradoxical behavior, making us ill if we do not eat them, while all other substances make us ill only when we do eat them. What food must contain to be wholesome is a question of primary interest to the cook rather than to the scientist. Accordingly the appreciation of results of

vitaminology are often out of all proportion to their scientific importance. Moreover, the vitamin nature of ascorbic acid could not contribute much to its real scientific interest, since its importance and presence in plant and animal tissues has been demonstrated already."

The author goes on to write: "Two years later I was condemned to be professor and sent to the chair (of biochemistry) in Szeged. At the same time fate has sent me a clever collaborator, J. L. Svirbely, who has had some experience in vitamin C tests and brought with him the convicion that my ascorbic acid could not be vitamin C. All the same I made him test my old suspicion to see whether the small quantity of powder left in the bottom of one of my tubes was not the vitamin C. In November 1931 he had definite evidence that it was. At this time also Tillmans directed attention toward the possible identity. We did not publish until we could repeat our experiment on a large number of animals. Simultaneously King and Waugh reported the isolation of crystals from lemon juice which had antiscorbutic properties and seemed to be identical with ascorbic acid, that time 'hexuronic acid.'"

The present volume is thus a personal account, projected against a background of related work by other investigators, of the researches of Szent-Györgyi, whose labors have led to such diverse results as the isolation of vitamin C and the discovery of the catalytic nature of malic, oxalo-acetic, succinic and fumaric acids.

The Biological Standardisation of the Vitamins. By Katharine H. Coward, D.Sc., Head of Nutrition Department, Pharmaceutical Society of Great Britain. Cloth. Price, $4.50. Pp. 227, with 44 illustrations. Baltimore: William Wood & Company, 1938.

This book supplies, in compact and readable form, much authoritative information which should be in the hands of all persons working in the field of biologic assay of the vitamins. It should also be interesting and valuable to those concerned solely with the interpretation of the results of biologic assay. The book is divided into two parts. Part I deals with the description and evaluation of a variety of technics proposed by different English and European investigators for the determination of vitamins A, B_1, C and D in terms of international units. This section provides many such useful and practical details as suggestions for the proper management of the rat colony, principles underlying the selection of satisfactory materials for use in both test and stock diets, prevention of "refection" and the most convenient methods for administration of the minute quantities of test materials which must frequently be employed. Part II deals with the mathematical estimation of the accuracy of the results obtainable for the different vitamins. The construction and proper use of curves of reference and response are clearly described by the author, who considers these devices economical of time and labor when the determination of the exact potency of the test material in numbers of international units per gram is required. An appendix contains a reprint of the report of the second conference on Vitamin Standardisation, London, 1934, in which the International Standard materials and the international units are defined. The usefulness of the book for American workers is, however, limited by the fact that many of the technics commonly employed by American investigators for the determination of the various vitamins are not discussed. In the United States, for example, the official methods described by the U. S. Pharmacopeia for the assay of vitamins A and D in terms of U. S. P. (equivalent to international) units differ in some respects from those used abroad. Also the methods most frequently used for the biologic assay of vitamins B_1 and C; i. e., the Sherman-Chase rat-growth method and the Smith rat-curative method for vitamin B_1 and the Sherman, LaMer and Campbell method for vitamin C, differ in considerable detail from those described by Coward. The reader must bear in mind the fact that a variety of technics may be used for the biologic assay of vitamins in terms of international units, the chief requirement being that a simultaneous test be run on the International Standard material whenever a determination of the vitamin potency of a substance is made. American workers will find it necessary to consult other references for the technical details of methods official in the United States.

Rancidity in Edible Fats. By C. H. Lea, B.Sc., Ph.D. Department of Scientific and Industrial Research, Food Investigation Special Report No. 46. Paper. Price, $1.10. Pp. 230, with 38 illustrations. New York: British Library of Information; London: His Majesty's Stationery Office, 1938.

This report is a review of the present state of scientific knowledge concerning the development of rancidity in edible fats and fat containing foods. The author defines rancidity as the deterioration in odor and flavor which develops in fats or in the fatty constituents of foods on keeping. Rancidity may occur as a result of the absorption of odors, the action of enzymes present in tissues, the action of micro-organisms, atmospheric oxidation or any combination of these. The book contains a brief but adequate discussion of each of these subjects. Methods of detecting and measuring rancidity are described. There is also a discussion of antoxidants, including the recent work of Mattill and Musher and others, and a bibliography of references to the literature. The book contains an initial chapter on the chemistry of fats and a final chapter on rancidity in dairy products and in the fat of meat. This report should prove useful to persons concerned with the preservation of foods and it is a fitting addition to the splendid monographs that have been issued under the auspices of the Food Investigation Board.

The International Cancer Research Foundation Report of Activities During 1937. Paper. Pp. 143. Philadelphia: The Foundation, [n. d.]

This volume summarizes the investigations assisted or supported by the foundation during 1937. It is especially interesting to those who are concerned with cancer research. Progress of each piece of work is described in full and the publications based on such work which appeared during 1937 are listed. The table of contents indicates the senior member of the research group receiving the financial help of the foundation. Financial statements indicate that the organization paid grants of more than $400,000 during 1937. The individual problems studied by the various workers cover all aspects of cancer research and are too numerous to mention even in general classifications. The funds of the organization are not used for buildings or equipment, but the foundation can accept gifts or contributions for such expenses. Between 35 and 50 per cent of the income of the foundation must be allotted outside the United States according to the by-laws of this foundation, which was organized in Philadelphia, June 8, 1932.

The Chicago Recreation Survey, 1937. Volume I: Public Recreation. Volume II: Commercial Recreation. A project sponsored jointly by the Chicago Recreation Commission and Northwestern University. By Arthur J. Todd, Chairman, Department of Sociology and Anthropology, Northwestern University. In collaboration with William F. Byron, Chairman, Division of Social Work, Northwestern University. Howard L. Vierow, Director, Chicago Recreation Survey. Conducted under auspices of the Works Progress Administration, National Youth Administration and Illinois Emergency Relief Commission. Boards. Pp. 268; 167, with illustrations. Chicago, 1937.

This voluminous report is the product of joint effort participated in by the Chicago Recreation Commission, Northwestern University, Works Progress Administration, National Youth Administration and Illinois Emergency Relief Commission. Volume I deals with public recreation, volume II with commercial recreation. In volume I will be found chapters dealing with the planning and historical aspects of public recreation, its administration, financing management, facilities, museums, forest preserves, facilities for golf and tennis, swimming, lagoons and harbors, public libraries and miscellaneous. Numerous charts, diagrams and maps in many colors illustrate and clarify the text. Tabulations abound, going into infinite detail as to numbers and character of equipment and personnel, as well as costs. Volume II deals with licensing and control of commercial recreation and with the various forms of these, such as motion picture theaters, legitimate, concert and operatic theaters, billiards and bowling establishments, baseball, basketball and football, boxing and wrestling, commercial health clubs, gymnasiums and natatoriums, horse racing, riding, polo and horse shows, bicycling and automobile racing, golf and tennis, ice sports and roller skating rinks, rental libraries, sight-seeing tours, observatories, air sight-seeing flights, excur-

sions, annual shows, conventions, radio, newspaper promotion stunts, amusement parks of every conceivable variety, ballrooms and dancing schools, retail liquor dispensing establishments, and commercialized vice. Maps, charts and tabulations are numerous and comprehensive.

There is a tremendous amount of reference material in these volumes. The work should serve as a valuable record of conditions as they exist in 1938, and it points the way to intelligent and constructive planning for future development. The most significant correlation established in the report is one that might have been anticipated and which is shown most graphically in the maps; namely, organized vice runs parallel with poor housing, liquor establishments and commercial "recreation" of the poorer types, and absence of adequate recreational facilities of the better type.

An Introduction to Chemistry. By John Arrend Timm, Assistant Professor of Chemistry, Fellow of Trumbull College, Yale University. With a foreword by John Johnston, Director of Research, United States Steel Corporation. International Chemical Series, James F. Norris, Ph.D., Consulting Editor. Third edition. Cloth. Price, $3.50. Pp. 568, with illustrations New York & London: McGraw-Hill Book Company, Inc., 1938.

The author has attempted to stress the philosophy of chemistry. The subject matter is logically presented in a style intended for those whose main interest lies in some other field. The scientific method, chemical literature, practical applications of chemical research and the history of chemistry are elaborated only so far as these contribute toward a general education. Many modern concepts, such as acid-base theory, radiation, nuclear chemistry and vitamin chemistry, are included, together with the classic experiments and theories of chemistry. The text contains references to books and original publications for collateral reading sufficient to stimulate but not burden the reader. The book is well illustrated and clearly printed. The volume is not suited to those who seek detailed chemical information.

Van Nostrand's Scientific Encyclopedia. Cloth. Price, $10. Pp. 1,234, with illustrations. New York: D. Van Nostrand Company, Inc., 1938.

A great volume of this type is an indication of the tremendous mass of scientific knowledge now assembled in many fields. In the development of this book ten contributing editors and eleven consulting editors have participated. Apparently the only physician concerned is Dr. R. Sterling Mueller, instructor in surgery in Columbia University. One finds many medical subjects rather inadequately treated. If one is to believe the initials at the end of the article on cancer, it was written by Warren K. Green, professor of astronomy at Amherst College, in collaboration with Dr. Mueller. Our absence of knowledge of certain phases of cancer would indicate that a professor of astronomy might be the ideal collaborator for such a purpose. The article dealing with carbuncles is written jointly by the geologist and the doctor because it turns out that a carbuncle is another name for a stone called a garnet. The discussion of syphilis makes no mention of the great campaign now under way in this country or of the standardized methods of treatment developed as a part of that campaign. Neither is there any reference to the gradually developing laws regulating marriage during syphilis. This volume offers sound information on most of the subjects that it discusses but not the type of information that one secures in encyclopedias in which great numbers of authorities take the responsibility for various branches of science.

Mount Sinai Hospital, Philadelphia: Diet Manual. Second edition. Paper. Pp. 87. Philadelphia, [n. d.].

The physician who is charged with prescribing a diet in any institution is between the difficulty of individualizing the diet for his patient and meeting the limitations set up by the needs of the occasion and the facilities of the institution. Thus it is important to have certain standards from which diets can be developed. There are a considerable number of books available which supply data concerning protein, carbohydrates and fats, mineral salts, vitamins and caloric value of ordinary portions of various foods. There are also a number of special works dealing with the development of diets for diabetic patients and those with dysentery, colitis, epilepsy and other conditions. The diet list prepared by the Mount Sinai Hospital, Philadelphia, includes all these data in mimeographed form as well as a number of other diets which continued usage in that institution has indicated are most frequently demanded. Those wishing a standardized list of this character will find the Mount Sinai notations exceedingly practical and suggestive.

Physicians of The Mayo Clinic and The Mayo Foundation. Cloth. Price, $10. Pp. 1,575, with portraits. Minneapolis: University of Minnesota Press; London: Oxford University Press, 1937.

This is the third of a series of volumes which have listed the physicians associated from time to time with the Mayo Clinic and the Mayo Foundation, providing for most of them a photograph, a brief biography and a bibliography. The volume thus constitutes an invaluable work of reference for all publishers and periodicals, since many of those concerned have made their names enviable as contributors to medical progress. The book is well arranged, nicely printed and in the mass of its material a useful work in the evaluation of the factors that make for medical success.

Milk and Nutrition: New Experiments Reported to the Milk Nutrition Committee. Part II: The Effects of Dietary Supplements of Pasteurised and Raw Milk on the Growth and Health of School Children (Interim Report). Paper. Price, 1s. 9d. Pp. 34. Shinfield, Reading, England: National Institute for Research in Dairying, 1938.

There are presented in this pamphlet the results of a study, conducted over a period of one school year, of the influence of milk on growth and health. The home diets of the children were not controlled. Four groups of 2,000 children each received supplements at school of, respectively, biscuits, one-third pint of pasteurized milk and two-thirds pint of either pasteurized or raw milk. It was found that the average child receiving milk grew slightly more in height and weight than the average child who did not receive supplements of milk at school. Children who received larger amounts of milk thrived somewhat better than those receiving smaller amounts. No significant difference was found with raw versus pasteurized milk. The differences between groups, however, are small, and the committee interprets this as evidence of improvements in the diets at home since Orr made his report in 1928.

Die Hypovitaminosen: Relative Vitaminmangel-Krankheiten in der Praxis. Von Prof. Dr. Richard Seyderhelm, Direktor der medizinischen Klinik am Hospital zum Heiligen Geist, Frankfurt a. M. Paper. Price, 8 marks. Pp. 156. Leipzig: Johann Ambrosius Barth, 1938.

Seyderhelm has produced a book which should be useful for clinicians who read German. Hypovitaminosis is considered to be either primary or secondary, primary when due to insufficient amounts of vitamins in the food and secondary when due to defective absorption or increased demands. The therapeutic use is discussed of preparations containing vitamins A, B_1, riboflavin and other members of the vitamin B complex, and vitamins C and D. Brief mention is made of vitamins E and P. A list of commercial vitamin preparations is provided. There is also a short table of foods which are useful as sources of the vitamins.

Artificial Light and Its Application. Commercial Engineering Department, Westinghouse Lamp Division, Westinghouse Electric & Manufacturing Company. Paper. Price, 75 cents. Pp. 258, with illustrations. Bloomfield, New Jersey, [n. d.].

This planographed report is an extensive discussion of artificial light and its application. There are chapters dealing with light sources, with "the language of lighting," photometry, light and vision, color, light control and lighting equipment, interior lighting design, industrial lighting, school lighting, commercial and public building lighting, display lighting, home lighting, farm lighting, floodlighting, recreational and sports lighting, architectural lighting, electrical advertising, street and highway lighting, and lighting in the theater. The list of topics will suggest the wide range of interests to which this report should appeal. To the ophthalmologist, the physician who is a member of the school board, the school physician and the school administrator, the chapters dealing with light and vision and the lighting of school rooms should be especially useful, as should the discussion of photometry. The report is comprehensive and detailed, liberally illustrated with

photographs and diagrams, and accompanied by extensive tables, charts and plans for the application of artificial light under virtually every conceivable set of circumstances from the feed alley in a horse barn to the majestic façade of a governmental building. The Better Light-Better Sight activity of recent date, which has sharpened interest in the subject of lighting and its relation to vision, and the consequent stimulus to interest in sight conservation, should create a demand for information which this book is admirably calculated to supply. Reports of this character are an example of how industries may furnish valuable contributions to health and welfare while at the same time promoting their own commercial interests.

Petting-Wise or Otherwise? By Edwin Leavitt Clarke. Paper. Price, 25 cents. Pp. 32. New York: Association Press, 1938.

For patients who prefer to take their sex education with a sugar coating, this pamphlet may be recommended as far as it goes. The information is conveyed through recital of the conversation between two young persons, married and engaged in campus leadership activities, and an older married couple, both physicians, during a call by the former at the home of the latter. Like all writing in this field which singles out one phase of the sex question, such as masturbation or petting, it suffers from lack of balance, in that it does not tell the whole story. What it does tell is sound and adequate, though the technic renders it much more wordy than would have been necessary to convey the information in simple straightforward style. The persistence of this style of writing about sex seems to be an indication that not all readers are willing to take their facts straight, a fact which might be commended to the attention of supermodern writers who are not content to call a spade a spade but must add details.

Keesing's Medical Digest, January 1—March 31, 1938. Fabrikold. Subscription price, £1. 5s. per annum. London: Keesing's Medical Digest, Ltd., 1938.

This small book has a calendar on the first page, followed by two vacant pages for telephone numbers and ninety-six pages of abstracts of articles published recently in various medical journals. Then follow many blank pages on which the physician may record his visiting list, with a few pages to record obstetric engagements, adjacent to the dates of the last menstruation, first fetal movements, and when labor is expected. The last pages also are blank to record the amount of cash receipts. The book is of the loose leaf type, fitting between spring covers which, when sprung backward, permit the easy removal of all the contents and its replacement with new material.

On Thought in Medicine (Das Denken in der Medizin). By Hermann von Helmholtz. An Address delivered August 2, 1877, on the Anniversary of the Foundation of the Institute for the Education of Army Surgeons. Introduction by Arno B. Luckhardt. [Reprinted from Bulletin of the Institute of the History of Medicine, Vol. VI, No. 2, February, 1938.] Boards. Price, 75 cents. Pp. 27, with portrait. Baltimore: Johns Hopkins Press, 1938.

In 1877 von Helmholtz delivered an address on the anniversary of the foundation of the Institute for the Education of Army Surgeons. In his introduction to the reprinting of this address Professor Luckhardt indicates that universality is proved by the fact that this same address might well have been written to meet conditions in the world within the last few years. The essay "On Thought in Medicine" is a recapitulation of medical theories of the past and a demand for scientific evidence from the laboratory and the clinic as the basis for medical progress.

Leaves from a Surgeon's Case-Book. By James Harpole. Cloth. Price, $2.75. Pp. 300. New York: Frederick A. Stokes Company, 1938.

The title almost expresses the character of this volume. It is written by a surgeon under a non de plume and is essentially a collection of anecdotes from medical practice, offering for the lay reader in this way educational material in an easily absorbable medium. There is not a sustained interest throughout the book but the casual reader will find that it offers so much of interest that he is likely to proceed gradually throughout the entire volume.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Death of Physician from Pneumonia Compensable.—The claimant's husband was surgeon-in-chief of the defendant hospital. On Jan. 29, 1933, at 12:30 a. m., he responded to an emergency call from the hospital. The weather was cold and windy, with snow and rain falling intermittently. The patient was found to be in an extremely critical condition, because of a bad fracture of the skull and a broken leg. According to the custom of the hospital, an incoming patient is observed in the dispensary, located in the basement, and if surgical attention is required he is removed to the operating room on the top floor of the hospital, unless the injury is of a very minor nature. The claimant's husband, evidently concluding that an immediate operation was necessary and that the patient should not be subjected to any avoidable disturbance, performed a major operation on the patient in the dispensary. The room temperature there was abnormally low, estimated as between 40 and 50 degrees. Although the physician, in the course of the operation requiring about an hour, had donned an extra gown, he had a severe chill. When the operation was completed, he was placed in a bed in the hospital and kept there the rest of the night. On January 31, in accordance with plans he had made, he started on a vacation but was taken ill en route and died in a hospital, February 28, "of influenza pneumonia and attending complications." The claimant sought compensation under the workmen's compensation act of Pennsylvania. The referee found that the death was the result of an accidental injury and awarded compensation, the award being affirmed by the workmen's compensation board. The court of common pleas reversed the finding of the board, and the claimant appealed to the superior court of Pennsylvania.

A nurse who assisted in the operation testified that she noticed that the physician's shoes and the bottom of his trousers were wet and that he told her "his car got stuck in the snow, in the slush, on the way up and he had to shovel his way out." The admission of this testimony was objected to on the ground that it was hearsay. Declarations of an injured person, said the court, made at or so near the scene of the accident and so shortly after it happened as to preclude the presumption that they were the result of premeditation or design are generally held to be admissible. Here the evidence did not warrant the slightest suspicion that the physician's statement was uttered with premeditation or with an ulterior purpose in mind. While it did not definitely appear, the court thought it could be reasonably assumed that a very brief time intervened between the physician's departure from home and his arrival at the hospital and that the statement was made to the first person he met. Furthermore, in the court's opinion the proof of an accidental injury did not depend entirely on the nurse's alleged hearsay testimony; there was competent evidence that she saw the physician's wet clothing. Owing to the inclement weather, with "awful driving conditions," it could readily be inferred from what the nurse observed that something of an unusual nature had happened to the physician on his way to the hospital. It was entirely safe to say that, in the ordinary course of events, a surgeon does not go to a hospital where he is to operate, with wet trousers and shoes. If such a thing occurs, one naturally concludes that he had some unusual experience.

Direct evidence of the cause of the physician's wet clothing was not necessary; it could be established by circumstantial evidence. Here, the court said, the physician met with an accident before he entered the dispensary. In view of the patient's critical condition, prompt action was evidently necessary. The humanitarian endeavor to save the life of a person who was so seriously injured could not be regarded in any other sense than one of absolute necessity, and not as a voluntary act performed under usual conditions. If pneumonia is contracted

by exposure to cold or water, under conditions which usually prevail, the general rule is that it is not compensable. On the other hand, if one is exposed in the course of his employment to unusual conditions, and pneumonia results therefrom, there is an accidental injury. The court thought it unnecessary to discuss the medical testimony but expressed the view that it was sufficient to establish the causal connection between the accident and the death. The proof of a wetting established a mishap—an untoward event, which was the superinducing cause of death. It was followed by exposure in an unusually cold room, where at that time it was vitally necessary for the physician in the course of his employment to perform an operation. The facts, in the opinion of the court, were sufficient to support the finding of the referee that there was an accidental injury within the meaning of the workmen's compensation act. The judgment of the court below was therefore reversed and the record remitted with directions for a judgment to be entered on the findings and conclusions of the workmen's compensation board.—*Roth v. Locust Mountain State Hospital (Pa.), 196 A. 924.*

Basic Science Acts: Health Lecturer Practices the Healing Art.—The defendant, Vivi Ann Mielke, also known as Vivi Ann Wyntor, was charged with practicing healing without a valid certificate of registration in the basic sciences. The trial court certified to the Supreme Court of Minnesota the following question: "Does the amended information as filed charge a public offense under the Basic Science Act of the State of Minnesota as set out in section 5705-1 et seq., Mason's Minnesota Statutes for the year 1927?"

The amended information charged the defendant with advertising herself as an assistant and staff lecturer for an osteopath of Kansas City and that she would give free daily lectures at specified times in a hotel in St. Paul. During the lectures the defendant solicited women present to attend a lecture course which was to follow immediately, for which a fee was charged. A number of women attended and paid the fee, and during the lectures certain products or concoctions were described by the defendant and their uses and values discussed. Circulars were distributed by and under the direction of the defendant which further described the products. It was announced, during the lectures, that the defendant had such products for sale and she suggested and recommended their purchase by the hearers. From the sales the defendant derived a commission of 55 per cent, the remainder going to the Kansas City osteopath, who held no license to practice healing in Minnesota. Among the products offered for sale were certain tablets claimed to contain red bone marrow and spleen and labeled "Useful in Secondary Anemia." The defendant also was charged with having sold female hormone tablets in connection with her lectures.

The basic science act of Minnesota, said the Supreme Court, forbids the practice of healing without first having obtained a certificate of proficiency in the basic sciences. By the terms of the act the basic sciences are defined to include anatomy, physiology, pathology, bacteriology, hygiene and chemistry so far as they relate to the human system or mind. The practice of healing is defined as including any person who shall in any manner for fee, gift, compensation or reward, or in expectation thereof, engage in the diagnosis, analysis, treatment, correction or cure of any disease, injury, defect, deformity, infirmity, ailment or affliction of human beings, or who for any fee suggests, recommends or prescribes any medicine or cure thereof. The defendant did not attack the constitutionality of the basic science act but asserted that as it applied to her or to the acts charged against her it infringed on her constitutional rights and that there was no relation between the requirements of the basic science act and the protection of the public as applied to her situation. With this contention, however, the Supreme Court disagreed. It is essential to the public health and safety, the court pointed out, that persons who, for compensation, suggest, recommend or prescribe medicine or treatment for the correction or cure of human ailments have a basic understanding of the subjects required by the basic science act. It is within the police power of the state so to require. According to the information lodged against her, the court continued, the defendant induced women to come to lectures for which she charged a fee and for those who had menstrual troubles she suggested and recommended tablets which she had for sale for correction and cure of their affliction. Her conduct, therefore, came squarely within the basic science act. The requirements of that act are germane to the safety and health of the public in the treatment of such ailments as those for which the defendant sold and recommended her tablets and medicines. Such being the case, no constitutional right of the defendant was infringed on.

In the opinion of the Supreme Court, therefore, the question certified by the trial court should be answered in the affirmative.—*State v. Mielke (Minn.), 277 N. W. 420.*

Dental Practice Acts: Board Exercises Administrative Functions in Revoking License.—A state board of dental examiners, said the district court of appeal, first district, division 1, California, exercises discretionary administrative functions, not judicial functions, in revoking licenses to practice dentistry. Neither a writ of prohibition nor a writ of certiorari, therefore, may be utilized to obtain a court review of a revocation order.—*Jacobs v. Board of Dental Examiners (Calif.), 75 P. (2d) 96.*

Society Proceedings

COMING MEETINGS

Academy of Physical Medicine, Washington, D. C., Oct. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.

American Academy of Ophthalmology and Oto-Laryngology, Washington, D. C., Oct. 9-14. Dr. William P. Wherry, 107 South 17th St., Omaha, Executive Secretary.

American Association for the Study of Goiter, Washington, D. C., Sept. 12-14. Dr. W. Blair Mosser, 133 Biddle St., Kane, Pa., Secretary.

American Association for the Study of Neoplastic Diseases, Washington, D. C., Sept. 8-10. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., Sept. 22-24. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 19-21. Dr. Daniel B. Moss, 547 W. Jackson Blvd., Chicago, Secretary.

American College of Surgeons, New York, Oct. 17-21. Dr. George W. Crile, 40 East Erie Street, Chicago, Chairman, Board of Regents.

American Congress of Physical Therapy, Chicago, Sept. 12-15. Dr. Richard Kovacs, 1100 Park Ave., New York, Secretary.

American Hospital Association, Dallas, Texas., Sept. 26-30. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.

American Public Health Association, Kansas City, Mo., Oct. 25-28. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23. Dr. Carleton B. Peirce, University Hospital, Ann Arbor, Mich., Secretary.

Associated Anesthetists of the United States and Canada, New York, Oct. 17-21. Dr. F. H. McMechan, 318 Hotel Westlake, Rocky River, Ohio, Secretary General.

Association of Military Surgeons of the United States, Rochester, Minn., Oct. 13-15. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.

Central Association of Obstetricians and Gynecologists, Minneapolis, Oct. 6-8. Dr. William F. Mengert, University Hospitals, Iowa City, Secretary.

Clinical Orthopedic Society, Nashville, Tenn., and Birmingham, Ala., Oct. 7-8. Dr. H. Earle Conwell, 215 Medical Arts Bldg., Birmingham, Ala., Secretary.

Colorado State Medical Society, Estes Park, Sept. 7-10. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

Delaware, Medical Society of, Dover, Oct. 10-12. Dr. Allan V. Gilliland, Smyrna, Secretary.

Idaho State Medical Association, Sun Valley, Sept. 6-10. Dr. Harold W. Stone, 105 North Eighth St., Boise, Secretary.

Indiana State Medical Association, Indianapolis, Oct. 4-6. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kentucky State Medical Association, Louisville, Oct. 3-6. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Detroit, Sept. 19-22. Dr. L. Fernald Foster, 311 Center Ave., Bay City, Secretary.

Mississippi Valley Medical Society, Hannibal, Mo., Sept. 28-30. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Nevada State Medical Association, Reno, Sept. 23-24. Dr. Horace J. Brown, 120 N. Virginia St., Reno, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 24-28. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.

Pacific Association of Railway Surgeons, Los Angeles, Oct. 7-8. Dr. W. T. Cummins, Southern Pacific General Hospital, San Francisco, Secretary.

Pennsylvania, Medical Society of the State of, Scranton, Oct. 3-6. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Vermont State Medical Society, Burlington, Oct. 6-7. Dr. B. F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Virginia, Medical Society of, Danville, Oct. 4-6. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 14-16. Mr. J. G. Crownhart, 119 East Washington Ave., Madison, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

8: 383-470 (July) 1938

Clinical Pathology Today. C. W. Maynard, Pueblo, Colo.—p. 383.
Elliptic Erythrocytes in Human Blood. J. K. Miller and M. A. Lucas, Louisville, Ky.—p. 391.
*Leukocytosis Associated with Acute Inflammation. A. Nettleship, Nashville, Tenn.—p. 398.
Focal Fatty Change of Liver and Focal Cirrhosis. H. L. Stewart, D. R. Morgan and V. L. Sprenkel, Philadelphia.—p. 405.
Cystadenoma Lymphomatosum. A. W. Freshman and S. K. Kurland, Denver.—p. 422.
Syphilis as Factor in Bioscopical Diagnosis of Adult Cervical Lymphadenopathy. H. Fox, Philadelphia.—p. 431.
Tularemia of the Human Breast. M. J. Kilbury and S. C. Fulmer, Little Rock, Ark.—p. 436.
Disseminated Echinococcosis. O. O. Williams, San Francisco.—p. 442.

Leukocytosis with Acute Inflammation. — Nettleship studied the relation of acute inflammatory lesions to the concurrent leukocytosis by producing small lesions in the skin of the rabbit. Streptococci introduced into the skin of the normal rabbit produced acute inflammation accompanied by an early severe, prolonged leukocytosis. Cytoplasmolysis of leukocytes at the site of injection set in within two hours after injection and became more marked during the first twenty-four hours of inflammation, at which time the most rapid increase of leukocytes occurred. The cytoplasm of the leukocytes was the only tissue which necrosed early. Necrosis of the other tissues involved in the abscess did not occur to any extent until after twenty-four hours. The mechanism which may be responsible for generalized leukocytosis with acute inflammation is that some breakdown product from the action of the injuring agent on peripheral tissue diffuses into the blood stream to cause leukocytosis and hyperplasia of the bone marrow.

American Journal of Diseases of Children, Chicago

56: 1-234 (July) 1938

Past Presidents of the American Pediatric Society (1888-1938): President's Address. K. D. Blackfan, Boston.—p. 1.
Vitamin A, Carotene and Vitamin C Content of Canned Milk. O. Meulemans and J. H. De Haas, Batavia, Java, Netherland East Indies.—p. 14.
Hepatomegaly in Juvenile Diabetes Mellitus Treated with Pancreatic Extract. H. G. Grayzel and L. S. Radwin, Brooklyn.—p. 22.
Size of the Heart in Healthy Children: Roentgen Measurements of Cardiac Area and Transverse Diameter for Sixty-Seven Children Between Birth and Age of Six Years. M. M. Maresh and A. H. Washburn, Denver.—p. 33.
Basal Metabolism of Undernourished Girls. F. B. Talbot, Boston.—p. 61.
*Serum Cholesterol in Patients with Rheumatic Fever: Further Study. F. M. Offenkrantz, Newark, N. J.—p. 67.
Respiratory Metabolism in Infancy and in Childhood: XXI. Daily Water Exchange of Normal Infants. S. Z. Levine, M. A. Wheatley, T. H. McEachern, H. H. Gordon and E. Marples, New York.—p. 83.
Acute Infectious Gingivostomatitis ("Vincent's Stomatitis"). W. C. Black, San Diego, Calif.—p. 126.

Serum Cholesterol in Rheumatic Fever.—Offenkrantz determined the serum cholesterol of 100 patients with rheumatic fever. Forty-nine of these were used as control subjects, since they had no evidence of rheumatic activity at the time. Evidence of such activity consisted of elevation of the leukocyte count above 10,000 per cubic millimeter, an erythrocyte sedimentation rate above 12 mm. per minute and increasing cardiac damage. The mean total value of the serum cholesterol (and standard deviation) was 181.9 ± 23.5 mg. per hundred cubic centimeters; the mean value of the free serum cholesterol was 50.5 ± 7.4 mg.; the mean percentage of free cholesterol was 27.3 ± 2.23. Of the remaining fifty-one patients, five died. Analyses of serum cholesterol one day before or ten minutes after death revealed severe depletion of the cholesterol ester and only slight lowering of the free cholesterol level, so that the percentage of free cholesterol rose above 30 in each instance. In eleven children who seemed to suffer activity of the rheumatic fever throughout the period (two summers) of observation the total cholesterol levels of the serum seemed to be definitely lowered and the percentage of free cholesterol elevated, so that the depletion was ascribed to the ester fraction. In twelve other patients the status of the disease fluctuated, periods of rheumatic inactivity being interrupted by flare-ups. The periods of activity again showed the lowered serum cholesterol level with the elevated percentage of free cholesterol (loss of ester). A general inverse relation was noted between the severity of the ester depletion (with a rise in the percentage of free cholesterol) and the sedimentation time. In nine cases, periods of cardiac decompensation were associated with the rheumatic infection. During such periods of failure the flare-up failed to produce the usual rise in the percentage of free cholesterol, although there was a moderate fall in the total cholesterol values. A similar situation seemed to prevail in seven cases in which a fluctuating status of the disease was complicated by a positive Mantoux reaction, though in six there was no evidence of active tuberculosis. Five instances are cited in which unusually high values for total cholesterol prevailed, despite activity of the disease. Possibly a psychiatric-functional status is associated with a particular type of cholesterol level in the blood.

American J. Obstetrics and Gynecology, St. Louis

36: 1-182 (July) 1938. Partial Index

Histologic Correlationship of Endometrial and Cervical Biopsies, with Comments on Etiology of Endocervicitis. A. Wollner, New York.—p. 10.
Causes of Vaginal Bleeding and Histology of Endometrium After the Menopause. H. C. Taylor Jr. and R. Millen, New York.—p. 22.
*Chemical Test for Pregnancy Applied to Determination of Estrin in Urine of Normal and Toxemic Patients in the Last Trimester of Pregnancy: II. Application of Short Chemical Method and Administration of Theelin in Late Toxemias of Pregnancy. J. E. Savage, H. B. Wylie and L. H. Douglass, Baltimore.—p. 39.
Pregnancy and Tuberculosis: Study of End Results. E. M. Jameson, Saranac Lake, N. Y.—p. 59.
Effect of Estrogenic Hormone on Contractility of Fallopian Tubes. S. H. Geist, U. J. Salmon and M. Mintz, New York.—p. 67.
Nonprotein, Urea and Rest Nitrogen of Blood During Labor and Puerperium. J. F. Cadden and A. M. Faris, New York.—p. 77.
Gynecologic Features of Carcinoma of Large Bowel. J. Schwartz and H. Bergman, New York.—p. 85.
Pitocin in Third Stage of Labor. M. R. White, Detroit.—p. 90.
*Bilirubin Liver Function Test in Toxemias of Pregnancy. R. A. Lyon, Washington, D. C.—p. 99.
Potential Bisexual Character of Ovary: Preliminary Report. A. J. Ramsay and J. F. McCahey, Philadelphia.—p. 104.
Virilism and Female Pseudohermaphroditism with Relation to Bisexual Nature of Ovary. J. F. McCahey and A. J. Ramsay, Philadelphia.—p. 108.
Evaluation of Anterior Pituitary-like Substance Intradermal Test for Pregnancy: Study of Possible Relation of This Test to Prolan Content. J. J. Friedman and H. Fink, Brooklyn.—p. 116.
Arsenical Encephalitis During Pregnancy. C. Kuehn, R. A. Keating and E. von Haam, Columbus, Ohio.—p. 122.
A Five Year Study of Eclampsia in Maryland. J. M. Reese, Baltimore, and F. W. Peyton, Lafayette, Ind.—p. 130.
Erythroblastosis. L. M. Hellman and A. T. Hertig, Boston.—p. 137.

Chemical Test for Pregnancy.—Savage and his associates made frequent examinations of the urine, blood pressure, eyegrounds, chemical determinations of the blood and renal function of fifty-eight toxemic patients admitted to the University Hospital in the last trimester of pregnancy. Twenty-four hour urine specimens were collected and estrogenic determinations were made. A few normal cases were included in order to establish normal levels of estrogenic excretion. A modification of the Schmulovitz and Wylie test for the chemical diagnosis of pregnancy by the detection of estrogen in the urine was devised. The procedure follows the principles of the original test with a few minor changes but uses only one tenth of the twenty-four hour specimen of urine. A marked reduction in the time required for the laboratory performance of this test, of from twenty-four to thirty hours to four hours, has thereby been achieved. Excretion of estrogen is expressed in terms of the "ferric chloride number," which is obtained as follows: The final colored alcoholic layer containing the estrogen extracted from the specimen of urine is filtered into a colorimeter cup and set at 10 mm. and is com-

pared with a standard 33 per cent ferric chloride solution, the reading of which is the ferric chloride number. The final reading in millimeters is multiplied by 10, and the factor 9 (the blank error is 1 mm.) is subtracted to give the final ferric chloride number. The excretion of estrogen expressed as ferric chloride numbers was 87.16 in six normal pregnant subjects, 47.05 in twenty-six patients with chronic nephritis complicating pregnancy and 40.03 in twenty-six cases of preeclampsia. Nine patients received 10,000 international units of theelin intramuscularly on each of three successive days and no improvement took place which could be ascribed directly to the hormone therapy.

Bilirubin Test in Toxemia of Pregnancy.—Lyon determined the function of the liver by the bilirubin elimination method in twenty cases of abnormal pregnancy (eclampsia, preeclamptic toxemia, nephritic toxemia, vomiting of pregnancy and premature separation of the placenta). The average retention was 11.8 per cent. He states that toxemias of pregnancy cannot be nosologically arranged on the basis of the bilirubin hepatic function test. However, the procedure is probably the most readily adaptable measure of the labile and manifold functioning liver. As such it may be of value together with renal function tests to aid in establishing a delimiting zone between the nephritic and preeclamptic toxemias.

American Journal of Public Health, New York

28: 807-906 (July) 1938

Investigation of Early Syphilis. W. T. Clark and C. A. Sargent, Buffalo.—p. 807.
Nutrition Services in Maternal and Child Health Programs Under the Social Security Act. Marjorie M. Heseltine, Washington, D. C.—p. 813.
Accuracy of Cancer Death Records. Eleanor J. Macdonald, Boston.—p. 818.
Precision Methods in Determination of Heavy Metals. L. T. Fairhall, Washington, D. C.—p. 825.
Formate Ricinoleate and Brilliant Green Bile Broths to Detect Coliform Organisms in Pasteurized Milk. I. C. Gunsalus and C. N. Stark, Ithaca, N. Y.—p. 832.
Politics in Selection of Health Department Personnel: Is There a Remedy? W. P. Capes, Albany, N. Y.—p. 835.
Sanitary Study of Commercial Laundry Practices. L. Arnold, Chicago.—p. 839.
Supervision of Food in New York City. A. Lichterman, New York.—p. 845.
The Nutritionist in a City Public Health Program. Sophia S. Halsted, Detroit.—p. 849.
Schick Reactions in Students of Medicine. H. C. Pulley and M. S. Fleisher, St. Louis.—p. 854.
Evaluation of Dental Programs for Children. J. M. Wisan, Elizabeth, N. J.—p. 859.

American Journal of Surgery, New York

41: 1-186 (July) 1938

Clinical Study of Pulmonary Embolism: Analysis of 146 Fatal Cases. H. Robertson, Philadelphia.—p. 3.
Anesthesia for Thyroidectomy. G. Crile Jr. and L. E. Adams, Cleveland.—p. 22.
Treatment of Acute Cholecystitis. H. P. Totten, Los Angeles.—p. 29.
Observations on Clinical Employment of Pituitary and Pituitary-like Gonadotropic Principles in Certain Conditions Characterized by Failure of Ovulation. E. C. Hamblen, Durham, N. C.—p. 35.
*Endocrines and Their Relationship to the Breast. C. H. Birnberg, L. Kurzrok and S. Livingston, Brooklyn.—p. 39.
New Surgical Procedure in Treatment of Prolapse of Uterus and Bladder. W. E. Mowery, Salina, Kan.—p. 42.
Hemorrhoidectomy with High Frequency Electric Current. E. E. Arnheim, New York.—p. 45.
*Clinical Results Following Use of Surgical Jelly Containing Maggot Active Principle: Preliminary Report. S. K. Livingston, Hines, Ill.—p. 49.
Relation of Trauma of the Hand to Occupation. N. E. Eckelberry, New York.—p. 51.
Surgery of Ambulatory Patient. L. K. Ferguson, Philadelphia.—p. 57.
Skin Graft for Ambulatory Patient. F. L. Smith, Rochester, Minn.—p. 67.

Endocrines and the Breast.—Birnberg and his associates treated fourteen cases of various breast dyscrasias (pain, nodules). Investigation included serial determinations of the gonadotropic substance and theelin and endometrial biopsies. There were eight cases of theelin deficiency, two of increased theelin production, two cases of deficiency of the corpus luteum hormone, one case of hypothyroidism and one of gynecomastia. The patients responded to therapy with the specific hormone shown to be lacking.

Clinical Results with Maggot Jelly.—During the last three years Livingston has used a surgical jelly containing the active maggot principle in the treatment of indolent ulcers of all types, carbuncles, boils, abscesses, compound fractures, burns of all types, preoperative and postoperative treatment of hemorrhoids, anal fissures and fistulas, cutaneous lesions with or without infection, infections of the cervix and genito-urinary tract and cutaneous grafts. The jelly is efficient, he believes, in chronic infections which are slow to heal and in which relief from local irritation is important and growth stimulation a necessity. The jelly, as the result of its chemical and its 5 per cent maggot content, relieves irritation and pain and is growth stimulating. In abscesses, boils and carbuncles a more rapid localization of the lesion and rapid postoperative healing occurred. Quick relief from pain, increased sloughing and earlier healing ensued in the various burns. In anal fissures and fistulas, healing was more rapid and the convalescence less painful after surgery. When the jelly is used preoperatively in hemorrhoids, bleeding is checked, irritation is relieved and spasm of the sphincter is released. When used postoperatively there are more rapid healing and less painful convalescence. More rapid granulation than with other ointments or jellies and relief from pain is obtained in indolent ulcers. Relief from irritation, softening of lesions, healing of fissures and dissolution of scaling occur in cutaneous lesions.

Archives of Neurology and Psychiatry, Chicago

40: 1-226 (July) 1938

Structure of Filum Terminale. I. M. Tarlov, Brooklyn.—p. 1.
Encephalographic Findings in Cases of Athetosis and Related Disorders. T. J. Putnam and T. J. C. von Storch, Boston.—p. 18.
Sweat Secretion in Man: II. Anatomic Distribution of Disturbances in Sweating Associated with Lesions of Sympathetic Nervous System. C. F. List and M. M. Peet, Ann Arbor, Mich.—p. 27.
Vesical Abnormalities Associated with Parkinsonian Syndrome. O. R. Langworthy, Baltimore.—p. 44.
*Cevitamic Acid Content of Blood Plasma in Alcoholic Psychoses. L. Alexander, M. Pijoan, P. G. Schube and M. Moore, Boston.—p. 58.
Variations in Magnesium and Potassium Associated with Essential Epilepsy. A. D. Hirschfelder and V. G. Haury, Minneapolis.—p. 66.
Method of Testing Cortical Function and Sensitivity of Skin: Aid in Differentiating Organogenic and Psychogenic Disturbances. W. H. Gantt, Baltimore.—p. 79.
*Dangerous Effects of Thorotrast Used Intracranially, with Special Reference to Experimental Production of Hydrocephalus. R. M. Stuck and D. L. Reeves, Montreal.—p. 86.
Metabolic Studies During Insulin Hypoglycemia Therapy of Psychoses. M. M. Harris, J. R. Blalock and W. A. Horwitz, New York.—p. 116.
Effects of Hypoglycemia and Anoxia on the Central Nervous System: Basis for Rational Therapy of Schizophrenia. E. Gellhorn, Chicago.—p. 125.
Clinical Results with Elsberg's Olfactory Test. A. Adler and K. H. Finley, Boston.—p. 147.
Hypertrophic Interstitial Neuritis with Papilledema. A. W. Diddle and R. L. Stephens, Iowa City.—p. 151.
New Modifications of Benzidine Stain for Study of Vascular Pattern of Central Nervous System. Margaret M. Doherty, T. H. Suh and L. Alexander, Boston.—p. 158.

Ascorbic Acid of Blood in Alcoholic Psychoses.—Alexander and his associates determined the ascorbic acid content of the plasma in 106 patients suffering from alcoholic psychoses and fifty-eight psychotic subjects, as controls. The essential difference between the subjects used as controls and the group of patients with alcoholic psychoses was that the latter presented a history of severe alcoholism of long standing with, presumably, a poor dietary regimen. The average ascorbic acid value for the sixty-five patients with alcoholic psychoses with polyneuritis was 0.576 mg. per hundred cubic centimeters, for the eighteen patients with alcoholic psychoses with slight or no polyneuritis the average ascorbic acid value for the plasma was 0.559 mg. per hundred cubic centimeters, and in twenty-three patients in whom the psychoses were only possibly precipitated by alcoholism the average ascorbic acid content of the plasma was 0.92 mg. per hundred cubic centimeters. The patients used as controls who were studied shortly after admission had an average for the ascorbic acid content of the plasma of 0.893 mg. per hundred cubic centimeters. Control patients who by refusing food had decreased their vitamin C intake and aged persons with psychoses had ascorbic acid values in the range of those for subclinical scurvy.

Dangerous Effects of Colloidal Thorium Dioxide.—Stuck and Reeves carried out experiments on cats, dogs and monkeys demonstrating hydrocephalus, precipitation and concentration of thorium dioxide (thorotrast) in the dependent parts, radioactivity and little if any elimination. In addition, the distribution of the compound was observed in the subarachnoid spaces by x-ray and histologic methods and its excretion from the subarachnoid space was studied. When the compound is injected into an animal, the material is treated as a foreign body, picked up by cells of the reticulo-endothelial system and stored. Its prolonged storage in the tissues of the body leads to mild and later to intense fibrosis. In white rats this has been followed by sarcoma. The great specific gravity of this substance is important when it is injected into the subarachnoid space, where it tends to become concentrated in the dependent portions. Of the three ionizing rays emitted by thorium, the alpha ray (or particle) is by far the most destructive. Its destructive action appears to be due to its intense ionization. Since the effect of the alpha ray is blotted out by less than 1 mm. of tissue, it is only by the injection or ingestion of radioactive substances that this ray becomes important. Hydrocephalus has been demonstrated in cats, dogs and monkeys after spinal, cisternal and ventricular injections of colloidal thorium dioxide. After ventricular injection no excretion of this material from the cranial cavity could be shown by x-ray or electroscopic examination of excreta and microscopic study of tissues. Because of the permanence of colloidal thorium dioxide in the subarachnoid space, with the continuous opportunity for its radioactive destructive effect and the development of areas of fibrosis and cicatrices, the clinical application of the material for encephalography and ventriculography is dangerous.

Archives of Otolaryngology, Chicago

28: 1-152 (July) 1938

Osteomyelitis of Frontal Bone: Report of Eight Cases. R. McKinney, Memphis, Tenn.—p. 1.
*Preoperative Management of Acute Streptococcic Mastoiditis. E. M. Atkinson, New York.—p. 10.
Osteoma of the Mastoid Process. S. A. Friedberg, Chicago.—p. 20.
Osteoma Growing from the Mastoid Cortex. G. M. Coates, Philadelphia. —p. 27.
Plastic Repair After Removal of Extensive Malignant Tumors of the Antrum. F. A. Figi, Rochester, Minn.—p. 29.
Improvement of Hearing in Cases of Otosclerosis: New One Stage Surgical Technic. J. Lempert, New York.—p. 42.
Nasal Allergy. A. H. Rowe, San Francisco.—p. 98.
Use of Hyoid Bone as Graft in Laryngeal Stenosis. E. A. Looper, Baltimore.—p. 106.
New Method of Operation for Congenital Atresia of Posterior Nares. J. C. Donnelly, Philadelphia.—p. 112.

Preoperative Management of Streptococcic Mastoiditis.—In mastoiditis in the course of an epidemic of influenza, of infection of the upper part of the respiratory tract or of a specific fever, according to Atkinson, the organism is nearly always a streptococcus of a virulent strain, usually hemolytic. A serious complication has never been warded off in a case of streptococcic infection by premature surgical intervention. The onset of complications is only hastened by surgical intervention before the infection has been brought under control and localized. Patients with mastoiditis are suffering, at the best, from bacteremia, if not active septicemia and they need physical and mental rest. Nothing can give that to them better than morphine. The diet is fluid, and extra fluid should be forced. Local heat should be used to relieve pain and to increase the blood supply. Specific serum is used in streptococcic disease. The serum must be polyvalent and of known potency and the dose must be adequate. In an adult with a severe infection 40 cc. intravenously is not too much for an initial dose. Serum should be continued in half doses, intramuscularly, at first daily and then every second day until the infection is brought under control. Nucleinic acid stimulates leukocytosis and may be given intramuscularly every second day, in alternation with serum. Strychnine and sodium cacodylate can be added for their tonic effects. In the absence of a satisfactory serum, blood transfusion should be employed and preferably an immunotransfusion. The quantity given should not be more than 250 cc. for an adult, for it is not difficult to overload an acutely intoxicated heart. Sulfanilamide and allied compounds must be used with discretion and with due appreciation of their limitations. There is so far no convincing evidence that the drug is of value in combating any streptococcus that is not hemolytic. From seven to ten days after the onset of the infection of the mastoid a change begins to be apparent in the patient. He who previously has been apathetic and listless becomes bright and alert; the sallow skin becomes clear, the dry, furred tongue clean and moist, the temperature falls from 103 or 104 F. to normal in the morning and 100 to 101 F. in the evening, while the pulse steadies, the blood picture (which possibly showed leukopenia at first) now shows leukocytosis and the tenderness of the mastoid, which was diffuse, becomes more definitely localized. The changed clinical picture should be allowed to stabilize itself and the temperature to settle or to take on a definite swinging character for two or three days before operation is undertaken. Operation then will reveal the presence of pus, probably localized in a cavity, in any event with the limits of its extent clearly defined; the postoperative course will be smooth and free from anxiety, and healing will take place rapidly. Of nineteen patients operated on without delay from 1926 to 1931, eight had complications, three of whom died, while of fourteen patients treated expectantly between 1932 and 1935 only one had any complication and none died. The average length of stay in the hospital for the first group was thirty-three days, and that for the second only twenty-seven days.

Archives of Physical Therapy, Chicago

19: 385-448 (July) 1938

Treatment of Gonococcic Arthritis with Artificial Fever. W. M. Solomon and R. M. Stecher, Cleveland.—p. 389.
Scope of X-Ray Therapy in Dermatology. E. P. Zeisler, Chicago.—p. 392.
Electrosurgery of Cervix After Six Years. M. L. Stadiem, New Orleans. —p. 398.
Cervicitis-Vaginitis Syndrome Therapy. M. A. Roblee, St. Louis.—p. 402.
Uterosalpingography and Transuterine Insufflation in Relation to Diathermy. G. Lyford, Cincinnati.—p. 408.
Diathermy in Coronary Thrombosis. W. W. Blackman and J. L. Richardson, Atlanta, Ga.—p. 412.
Exercise in Treatment of Chronic Cardiovascular Disease. L. F. Bishop Jr., New York.—p. 415.
Ultraviolet in Skin Infections. J. R. Scholtz, Los Angeles.—p. 419.
Present Status of Treatment of Arthritis. M. F. Lautman, Hot Springs National Park, Ark.—p. 426.

Illinois Medical Journal, Chicago

74: 1-96 (July) 1938

Individual Disease. G. Draper, New York.—p. 73.
Treatment of Pneumonia. E. B. Freilich and G. C. Coe, Chicago.—p. 80.
*Effect of *l*-Cevitamic Acid on Insomnia: Preliminary Report. S. Maurer, H. O. Wiles, E. W. Schoeffel, Chicago, and M. L. Fisher, Manteno.—p. 84.
Value of Irradiated Ergosterol in Treatment of Acne Vulgaris. Josephine Hinrichsen and A. C. Ivy, Chicago.—p. 85.
The Management of Pregnancy and Labor in Presence of Heart Disease. W. C. Danforth, Evanston.—p. 88.
Tuberculin Tests in a College Group. A. S. Webb, Chicago.—p. 92.

Effect of Ascorbic Acid on Insomnia.—Maurer and his associates have given from 1 to 3 Gm. of ascorbic acid daily to more than 100 patients suffering from insomnia and other conditions without evidence of toxic effect. Overdosage produces sound sleep from which the patient may be aroused easily, followed by drowsiness during the day. This drowsiness, however, disappears within twenty-four hours after the ascorbic acid has been discontinued. Administration of ascorbic acid was discontinued immediately on reports or observation of "apparently normal" sleep and not resumed until after the subjects again reported or were observed to be having difficulty in sleep. The beneficial effects of ascorbic acid lasted from a day to more than a week and varied with different individuals.

Iowa State Medical Society Journal, Des Moines

28: 261-372 (July) 1938

Medical Economics. A. M. Schwitalla, St. Louis.—p. 261.
Hypertrophy of Ligamentum Flavum as Factor in Production of Low Back and Sciatic Pain. W. D. Abbott, Des Moines.—p. 266.
Contact Dermatitis. L. J. Frank, Sioux City.—p. 271.
Fracture Dislocations of Lower Spine: Method of Reduction. V. A. Ruth, Des Moines.—p. 275.
Important Medicolegal Responsibility in Automobile Accidents. C. W. Ellyson, Waterloo.—p. 280.
The Goiter Heart. Irene A. Koeneke, Halstead, Kan.—p. 282.

Journal of Allergy, St. Louis

9: 433-534 (July) 1938

Activation of Ultrafiltrates of Ragweed Pollen Extracts by Means of Colloidal Substances. W. L. Long and Ida Teller, Philadelphia.—p. 433.
Specificity of Fungous Allergy. F. M. Rackemann, T. G. Randolph and E. F. Guba, Boston.—p. 447.
Influence of Epinephrine on Antigen and Antibody Action. L. Tûft, Philadelphia.—p. 454.
Method for Determining Pollen Concentration of the Air. E. C. Cocke, University, Va.—p. 458.
Studies with Antigens: I. Skin Reaction Curve Obtained with Serial Dilutions of Extracts. R. I. Dorfman, New Haven, Conn., and B. G. Efron, New Orleans.—p. 464.
*Hypersensitiveness to Tobacco and Biopsy Studies of Skin Reactions in Vascular Disease. J. Harkavy, New York.—p. 475.
Periarteritis Nodosa: Case Report. S. S. Berger and M. A. Weitz, Cleveland.—p. 489.
Effectiveness of Intravenous Hypertonic Sucrose and Adrenalin in Treatment of Status Asthmaticus. E. L. Keeney, Baltimore.—p. 497.
Insulin Hypersensitivity. A. E. Cohen and F. Simon, Louisville, Ky.—p. 503.
*Clinical Use of Phenylpropanolamine Hydrochloride (Propadrine) in Treatment of Allergic Conditions. W. E. Boyer, Philadelphia.—p. 509.
Relation of Age and Sex to Incidence and Prognosis in Phenylcinchoninic Hypersensitivity. D. A. Bryce, Plainfield, N. J.—p. 514.

Hypersensitiveness to Tobacco.—In order to determine the nature of the tissue response in patients with vascular disease Harkavy made biopsy studies of the area of skin reacting from the intracutaneous injections of tobacco extracts and wheals produced by saline and ragweed extracts used as controls in fifteen persons. Ten suffered from thrombo-angiitis obliterans, one had migrating phlebitis, one had coronary artery disease and three were surgical patients used as normal controls. Each of these patients was tested simultaneously with six different types of tobacco as well as ragweed, timothy, horse dander extracts and Coca's diluting fluid. Positive cutaneous reactions to tobacco were obtained in the twelve patients and in one of the control subjects. The type of reaction was characterized by an immediate urticarial wheal in ten of the patients and a delayed type of reaction in two. Of the three controls, one showed an immediate reaction to tobacco and ragweed and the other two were completely negative. Of the ten who gave immediate reactions, five had reagins to tobacco on passive transfer. Eosinophils, varying in numbers, were found in the histologic sections of the immediate urticarial wheals produced by the tobacco allergen in six of eight cases of thrombo-angiitis obliterans and in one case of migrating phlebitis. The biopsies of two patients with thrombo-angiitis obliterans and one with coronary artery thrombosis, in whom delayed reactions developed, showed an acute dermatitis. The exciting role of tobacco in the twelve patients observed was corroborated clinically by arrest in the progress of symptoms when the use of tobacco was discontinued. In one patient giving a delayed eczematous type of local reaction, a generalized eczema and exacerbation of the symptoms of thrombo-angiitis obliterans were induced by repeated subcutaneous injections of tobacco extract.

Phenylpropanolamine Hydrochloride in Allergy.—The propadrine that Boyer used in the treatment of forty-four instances of allergic conditions (asthma, urticaria and pollen asthma) was the hydrochloride of the racemic *dl*-form, melting point from 190 to 191 C. The salt is readily soluble in water, and aqueous solutions appear to be stable over long periods. Propadrine hydrochloride was used freely. As much as 0.05 Gm. was administered every two hours for five days or more without any toxic manifestations. Previously, the patients had been taking ephedrine or other drugs for the control of their symptoms. Four patients stated that propadrine hydrochloride was inferior to other forms of medication (usually ephedrine), five believed propadrine hydrochloride to be equally efficacious to previous medication and thirty-five patients reported that their greatest symptomatic improvement occurred with propadrine hydrochloride. Clinically, bronchial spasm, rhinitis and sneezing were relieved. There were no side reactions, so commonly encountered in the administration of ephedrine. In a large number of cases the patients derived marked relief without the usual manifestations of nervousness and insomnia, a frequent complaint of patients when using ephedrine. It is not necessary to administer sedatives with propadrine hydrochloride. It appears that propadrine hydrochloride may be used safely in cases of hypertrophy of the prostate. Tachycardia and palpitation, which have been fairly common symptoms associated with the administration of ephedrine, were not encountered in the present patients.

Journal of Bone and Joint Surgery, Boston

20: 559-824 (July) 1938. Partial Index

Results of Postural Reduction of Fractures of the Spine. R. Watson-Jones, Liverpool, England.—p. 567.
*Healing of Fractures of Atrophic Bones. J. Goisman and E. L. Compere, Chicago.—p. 587.
Recurrent Deformities in Stabilized Paralytic Feet: Report of 1,100 Consecutive Stabilizations in Poliomyelitis. C. H. Crego Jr. and H. R. McCarroll, St. Louis.—p. 609.
Bone Grafts in Ununited Fractures. M. S. Henderson, Rochester, Minn.—p. 635.
*Diagnosis and Treatment of Sacro-Iliac Conditions by Injection of Procaine (Novocain). K. O. Haldeman and R. Soto-Hall, San Francisco.—p. 675.
Sciatic Nerve and Piriformis Muscle: Their Interrelation a Possible Cause of Coccygodynia. L. E. Beaton and B. J. Anson, Chicago.—p. 686.
Cord Injury During Reduction of Thoracic and Lumbar Vertebral-Body Fracture and Dislocation. W. A. Rogers, Boston.—p. 689.
Treatment of Injuries of Cervical Spine. W. G. Crutchfield, Richmond, Va.—p. 696.
Ossification in Ligaments of Elbow Joint. St. J. D. Buxton, London, England.—p. 709.
Hemangiomas of Lower Extremities, with Special Reference to Those of Knee Joint Capsule and Phenomenon of Spontaneous Obliteration. J. B. Weaver, Kansas City, Mo.—p. 731.
Posterior Dislocation of Elbow Joint Complicated by Fracture of the Medial Epicondyle and Ulnar Nerve Injury. T. Outland and C. R. Hanlon, Sayre, Pa.—p. 750.
Curare Therapy for Release of Muscle Spasm and Rigidity in Spastic Paralysis and Dystonia Musculorum Deformans. M. S. Burman, New York.—p. 754.
Arachnodactylia: Report of Eight Cases. J. R. Norcross, Chicago.—p. 757.
Changes Simulating Legg-Perthes Disease (Osteochondritis Deformans Juvenilis) Due to Juvenile Myxedema: Report of Case. F. Albright, Boston.—p. 764.
Treatment of Birth Fractures of Femur. W. H. Robinson, Pittsburgh.—p. 778.

Healing of Fractures of Atrophic Bones.—Goisman and Compere endeavored to determine whether or not the fractures of atrophic bones unite at the same rate and to the same extent as fractures of normal bones of patients of similar ages. Ten cases of fracture and seventy-seven cases of osteotomy of atrophic long bones were studied. Too many variables were present to make possible a satisfactory scientific comparison or analysis; the impression gained was that union occurred as readily in fractures of atrophic bones as in fractures of bones of normal density. The osteotomies also healed promptly. In experiments, instead of attempting to produce regional atrophy by paralysis or immobilization, the authors attempted to bring about generalized wasting of bones both in adult and in young growing rats by reducing the intake of calcium. The rate and degree of fracture healing in these animals was compared with others on a normal stock diet or on a diet with excessive amounts of cod liver oil or calcium, or both. The observation of Clarke, Bassin and Smith that it is possible to produce atrophy of the bones of young growing rats by feeding a diet which is deficient in calcium, without the development of rickets, was confirmed. The changes in the skeleton caused by diets deficient in minerals are quite similar (although generalized) to the local atrophy of bone resulting from disuse, produced experimentally by Allison and Brooks. The addition of ammonium nitrate to the low calcium diet of adult rats failed to produce demonstrable atrophy. All fractures in adult rats in all the groups appeared to heal equally well. Definite roentgenographic and microscopic evidence of bone atrophy was obtained in the growing rats fed on a low mineral diet. Fractures of nonrachitic atrophic bone in clinical and experimental cases united as rapidly as did fractures in the normal controls, from which one may conclude that mesodermal tissue cells proliferate as well in the repair of a thin bone matrix as in that of a bone matrix of normal density, and perhaps sometimes more easily in the former. Fractures of bones in either young or old rats on diets deficient in mineral did not heal more promptly or more adequately when large amounts of vitamin D or calcium, or of both substances, were added to the diets than did those in rats which had been on a normal basic diet previous to fracture; in some instances these

supplements seemed to retard the repair of bone. Atrophy of the fractured bone, both in the low calcium group and in the group of rats on the stock diet, was consistently more marked than in the unfractured extremity of the same animals. This may be explained by the fact that for a period of about two weeks after fracture the limb was not used normally. The studies would seem to indicate that there is a normal mineral and vitamin threshold below which bones become atrophic. If the deficiency of vitamin D is marked, rickets also develops and fractures of the rachitic bones heal poorly. If the deficiency is largely of the mineral element, bones may become atrophic with no rachitic changes without affecting the rate of fracture healing, and the quality of union will be comparable to the quality of the bone fractured.

Sacro-Iliac Strains.—Haldeman and Soto-Hall treated forty-two consecutive patients in whom the diagnosis of probable sacro-iliac strain had been made by manipulation and the injection of procaine hydrochloride into the sacro-iliac joint. In order to prevent any possible reaction from the procaine hydrochloride, the patient is placed in the prone position and 0.2 Gm. of sodium amytal is given orally. From 20 to 30 cc. of a 1 per cent solution of procaine hydrochloride is injected. In cases of bilateral sacro-iliac strain, 15 or 20 cc. of the solution may be injected into each side. The best approach to the sacro-iliac joint requires the insertion of a long (spinal puncture) needle at a point over the sacrum midway between the two posterior superior spines of the ilium. The needle is then directed toward the desired side so as to make an angle of 45 degrees with the skin. At this angle the needle will pass between the lateral portion of the sacrum and the overhanging posterior superior iliac spine, through the fibers of the interosseous sacro-iliac ligament to the posterior margin of the sacro-iliac joint. The procaine hydrochloride is injected slowly while the needle is being inserted. After bony resistance is encountered, the needle is partially withdrawn and reinserted several times, so as to obtain a fan-shaped area of infiltration along the posterior aspect of the sacro-iliac joint. The needle should not be inserted at such an angle that it will pass superior to the upper margin of the sacrum. After five or ten minutes in which time local anesthesia takes place, manipulation of the sacro-iliac joints is carried out. Such manipulations include straight-leg raising, hyperextension of the hip with the knee flexed and the patient in the prone position, sudden traction on one leg while the other is fixed, and the method whereby with the patient in the supine position one shoulder is pressed against the table and the pelvis on the same side is rotated forward as far as possible. The lower part of the back is then strapped with adhesive tape and the patient reports back in a few days. In a few cases exacerbation of sciatic pain for a day or two following the manipulation required an analgesic. In a few instances in which relief was transitory the injection of procaine was repeated after one week, usually with additional improvement. The injection caused an immediate transient disappearance of signs and symptoms in most of the cases, and in 60 per cent the relief obtained was more lasting. This procedure affords a method of determining whether a disorder of the sacro-iliac joint is responsible for the patient's symptoms.

Michigan State Medical Society Journal, Lansing

37: 577-672 (July) 1938

The Doctor and a School Health Program. H. Cook, Flint.—p. 593.
The Venereal Disease Problem, Its Prevention and Control in Ingham County, Michigan. A. J. Aselmeyer and Lida J. Usilton, Washington, D. C.—p. 597.
Application of Survey to the Private Practitioner. H. L. Keim, Detroit.—p. 607.
Program for Control of Genito-Infectious Diseases in Ingham County, Michigan. R. S. Breakey, Lansing.—p. 611.
Survey of Syphilis in Oakland County for 1937: The Committee on Syphilis of the Oakland County Medical Society. H. R. Roehm, Birmingham; P. V. Wagley, J. D. Monroe, Pontiac, and E. E. Hammonds, Birmingham.—p. 618.
Six Months of Occupational Disease Reporting. J. M. Hepler, Lansing.—p. 621.
Decompression of the Small Bowel by Intestinal Tube Drainage at Site of Obstruction. C. G. Johnston, Detroit.—p. 623.
Review of Case of Thrombocytopenic Purpura Treated by Splenectomy. G. T. Aitken, Grand Rapids.—p. 628.

Military Surgeon, Washington, D. C.

82: 485-574 (June) 1938

Antiquity of Syphilitic Aneurysm. C. S. Butler.—p. 485.
*Hookworm Survey of CCC Enrollees. V. H. Cornell.—p. 491.
Use of Ozone in Treatment of Paradontosis. F. E. Frates.—p. 504.
Bullet in the Brain: Final Report. G. L. Johnson.—p. 511.
Acute Injuries: Physiotherapy as an Aid. H. P. Makel.—p. 515.
Anesthesia and Shock. A. Wineland.—p. 520.
Organization and Functions of Medical Services in Combined Operations of Land and Sea Forces. W. L. Mann and E. E. Hume.—p. 529.
Bilateral Cortical Necrosis of Kidneys: Case Report. O. O. Benson Jr.—p. 541.

Hookworm Survey of CCC Enrollees.—Cornell states that, of 1,079 CCC enrollees from the South, 597 (55.3 per cent) were found infested with hookworm. Following treatment, three successive specimens were found negative in 99.39 per cent of the 489 men examined. Samples of feces and soil beneath them, which had lain outdoors for several months in New York state, were found negative for hookworm ova and larvae. In the future it is believed that such a survey should be conducted by an independent laboratory group, working at successive collecting points throughout the area. This would speed up the survey so that fewer men would be discharged before treatment is given.

Missouri State Medical Assn. Journal, St. Louis

35: 233-298 (July) 1938

Missouri State Cancer Hospital: Its Relation to Medical Practice. P. F. Cole, Springfield.—p. 233.
Acute Mastoiditis with Surgical Procedure. W. B. Black, Kansas City.—p. 237.
Gonorrhea in the Male. J. R. Caulk, St. Louis.—p. 240.
Congenital Umbilical Hernia: Report of Case. J. G. Montgomery, H. M. Gilkey, F. B. Kyger and W. L. Jennings, Kansas City.—p. 244.
Hypoglycemic Treatment of Schizophrenia at Fulton State Hospital. F. A. Barnett, Fulton.—p. 246.
The Neuroses. J. F. McFadden, St. Louis.—p. 249.
Rubella and Encephalitis. A. S. Welch, Kansas City.—p. 251.

Nebraska State Medical Journal, Lincoln

23: 241-280 (July) 1938

Treatment of Advanced Malignancy. A. F. Tyler, Omaha.—p. 241.
Survey of Cancer of Breast at St. Elizabeth's Hospital 1928 to 1938. C. Johnson, Lincoln.—p. 245.
Avitaminosis as Likely Etiologic Factor in Polyneuronitis Complicating Pregnancy: Report of Case. R. Luikart, Omaha.—p. 247.
Pharmacologic Shock Treatment of Mental Disorders with Pentamethylentetrazol: Metrazol. J. C. Nielsen, A. H. Fechner and L. R. Nash, Ingleside.—p. 250.
Brucella Abortus Infection Treated with Sulfanilamide: Report of Case. L. T. Hall and R. L. Dunlap, Omaha.—p. 252.
Prostatic Obstruction in General Practice. C. A. Owens, Omaha.—p. 254.
Bedside Recognition and Treatment of Cardiac Irregularities. J. F. Gardiner, Omaha.—p. 258.

New England Journal of Medicine, Boston

219: 1-36 (July 7) 1938

The State of the Society: Report of the President. C. Frothingham, Boston.—p. 1.
Massive Hemorrhage from Peptic Ulcer. I. R. Jankelson and M. S. Segal, Boston.—p. 3.
Granulocytopenia Associated with Sulfanilamide Therapy. J. G. Allen and C. L. Short, Boston.—p. 6.
A Reappraisal of Vitamin D Milks. J. W. M. Bunker and R. S. Harris, Boston.—p. 9.

219: 37-74 (July 14) 1938

Further Experience with Regional Enteritis. C. G. Mixter and A. Starr, Boston.—p. 37.
*The Placental Transfer of Sulfanilamide. R. H. Barker, Boston.—p. 41.
Progress in Gastro-Enterology in 1936 and 1937. E. S. Emery Jr., Boston.—p. 42.

Placental Transfer of Sulfanilamide.—In order to determine the placental transfer of sulfanilamide, Barker analyzed samples of maternal venous blood (from seventeen pregnant women suffering from infectious diseases who had received the drug shortly before delivery) and of umbilical vein blood for free sulfanilamide content, according to the method of Marshall. He found that sulfanilamide given orally to the mother in labor is found in almost equal concentrations in maternal and fetal venous bloods. Apparently the placenta is freely permeable to the drug, and fetal complications from excessive maternal dosage are theoretically possible. No complications occurred in any of the infants of this group. The doses administered, however, were small in comparison with those that would be necessary in the treatment of severe maternal infections.

New Jersey Medical Society Journal, Trenton

35: 405-462 (July) 1938

Comprehensive Planning of Medical Care: I. Medicine in New Jersey Looks Forward. T. K. Lewis, Camden.—p. 409.
Id.: II. The Hospital's Responsibility in Comprehensive Planning for Medical Care. E. Frankel, Trenton.—p. 412.
Id.: III. Comprehensive Planning of Medical Care: The Responsibility of the Welfare Agency. S. Ewing.—p. 416.
A Plan for Adequate Medical Care for All: Plan Based on Coordination of Present Resources, Present Principles of Practice and the American Concept of Government. E. W. Sprague, Newark.—p. 420.
Hydatidiform Mole: Report of Case. O. R. Holters, Asbury Park, and H. Kazmann, Long Branch.—p. 423.
Treatment of Circulatory Diseases Based on Health Examination Procedure. C. W. Crampton, New York.—p. 426.
Maternal Welfare Article Number Twenty-Seven: Hemorrhage in Obstetrics. G. A. Braun, Newark.—p. 430.

Surgery, Gynecology and Obstetrics, Chicago

67: 1-152 (July) 1938

Allen B. Kanavel; Surgeon, Preceptor, Friend. S. L. Koch, Chicago.—p. 1.
The Personality of Allen B. Kanavel. C. A. Elliott, Chicago.—p. 5.
Electrocoagulation of 400 Cervical Erosions: A Photographic Study. Otillie Zelezny-Baumrucker and G. O. Baumrucker, Chicago.—p. 17.
*Renal Tuberculosis: Development of Renal Lesion. F. Lieberthal, Chicago.—p. 26.
Nonroutine Views in Roentgen Examination of Extremities. R. W. Lewis, New York.—p. 38.
Fertility and Sterility After Extra-Uterine Pregnancy. C. W. Mayo and E. O. Strassmann, Rochester, Minn.—p. 46.
*Renal Tuberculosis in Patients with Active Pulmonary Tuberculosis. E. M. Jameson, Saranac Lake, N. Y.—p. 56.
Influence of Certain Antispasmodic Drugs on Intestine of Man. R. J. Jackman and J. A. Bargen, Rochester, Minn.—p. 63.
Surgical Procedure for Total Thyroidectomy. E. C. Cutler and R. Zollinger, Boston.—p. 69.
Surgical Repair of Long Disabled Hand. F. Young, Rochester, N. Y.—p. 73.
Changes in Intracholedochal Pressure Following Cholecystectomy. C. B. Puestow, Chicago.—p. 82.
"Subdural" Hematoma. D. H. Kaump, Des Moines, Iowa, and J. G. Love, Rochester, Minn.—p. 87.
Reduction of Fracture Dislocations of Cervical Vertebrae by Skeletal Traction. L. G. Barton Sr., Plattsburg, N. Y.—p. 94.
Radical Breast Operation. H. C. Chase, New York.—p. 97.
*Hemorrhage from Carcinoma of Cervix: Control by Extraperitoneal Ligation of Hypogastric Arteries. M. L. Leventhal, A. F. Lash and A. Grossman, Chicago.—p. 102.
Brachioradialis Muscle Transposition for Triceps Weakness. F. R. Ober and J. S. Barr, Boston.—p. 105.
Retroperitoneal Pararenal Osteoma. H. L. Kretschmer, Chicago.—p. 108.
Amputation Stump of Arteriosclerotic Gangrene. F. W. Taylor, Indianapolis.—p. 114.

Renal Tuberculosis.—Lieberthal made a combined clinical and pathologic investigation of 270 cases of renal tuberculosis. In addition, postmortem studies and animal experiments were carried out to clear up certain problems which were not explained by clinical examination of the clinical cases. 1. The kidney shows a peculiar immunity to tuberculous infection by virtue of its rich blood supply and the large caliber of its capillaries. Hematogenic tuberculous infection of that organ becomes possible through the medium of embolism. 2. The initial lesions are situated mainly in the cortex and are usually bilateral. 3. In the spread of the tuberculous lesion through the kidney, three definite stages are evident: metastatic tubercles appear in the renal substance, a caseous ulcer appears on a renal papilla and a descending infection of the urinary mucous membranes follows and then an ascending reinfection of the previously uninvolved portions of the renal tissue occurs. 4. In this ascending reinfection of the renal tissue, the arterial system of the kidney plays a leading part. 5. Tuberculous strictures of the ureter and of individual calices lead to a stasis of tuberculous urine, which has a leading part in the maintenance and spread of the tuberculous process through the kidney. 6. This stasis also gives rise to hydronephrotic changes, which go hand in hand with tuberculous erosion to cause destruction of renal tissue. 7. Tuberculous lesions in the kidney have a tendency to heal, but as soon as the process breaks into and communicates with the lumen of the renal pelvis peculiar conditions are produced which counteract the tendency to heal. 8. Tuberculous lesions in the first stage are latent and cannot be diagnosed clinically. 9. Secondary nontuberculous changes which alter the final pathologic picture may occur in cases of renal tuberculosis.

Renal Tuberculosis in Pulmonary Tuberculosis.—Jameson declares that careful and repeated search for acid fast bacilli in smears of the sediment of a twenty-four hour specimen of urine should be made in every tuberculous patient who shows pus or albumin in the urine. Such smears, properly stained, will show acid fast organisms in a high percentage (28.4 per cent of 239 patients dying of active pulmonary tuberculosis) of positive cases. Doubtful cases and all those in which acid fast bacilli have been demonstrated should be further examined by guinea pig inoculation or culture. Renal tuberculosis was found to be three times as frequent in men as it is in women with pulmonary tuberculosis in this series, and in 76 per cent of these patients the lesions are bilateral. Patients with renal tuberculosis rarely have a "normal" urine, although the presence of tubercle bacilluria depends on the existence of a lesion in communication with the pelvis of the kidney.

Hemorrhage from Carcinoma of Cervix.—Leventhal and his associates performed bilateral extraperitoneal ligation of the hypogastric arteries in five cases for severe hemorrhage following maximal radiation therapy for carcinoma of the cervix. A few minor complications were experienced during the operative procedure in several instances. In one case the internal iliac vein was punctured and had to be ligated; in two cases metastatic glands were encountered along the large vessels, but these could be easily displaced to permit exposure of the hypogastric artery. No harmful changes occur in the bladder or rectum following ligation of the extraperitoneal hypogastric artery, because of the collateral circulation. This simple operation is followed by no primary mortality and is of value as a palliative measure or as the only procedure for uncontrollable hemorrhage from cervical carcinoma.

Yale Journal of Biology and Medicine, New Haven

10: 531-594 (July) 1938

Lyman Hall—Yale 1747: A Connecticut Doctor Who Mixed Medicine and Politics in Georgia. J. Krafka Jr., Augusta, Ga.—p. 531.
Bio-Electric Correlates of Methylcolanthrene-Induced Tumors in Mice. H. S. Burr, L. C. Strong and G. M. Smith, New Haven, Conn.—p. 539.
Relation of Toxoid Dilution to Immunizing Capacity. J. A. Bliss, New Haven, Conn.—p. 545.
Tetany of the Newborn: Case. Ethel Walker, New Haven, Conn.—p. 549.
*Yeastlike Fungi of the Human Vagina. L. Weinstein and L. J. Wickerham, New Haven, Conn.—p. 553.
Blood Hydrogen Ion Concentration in Vivo: II. Effects of Acids, Salts, Dextrose and Adrenalin. C. Marshall and L. F. Nims, New Haven, Conn.—p. 561.
Ovarian Hormones in Relation to Female Genital Cancer. E. Allen, New Haven, Conn.—p. 565.
Method of Laminar Thermocoagulation of Cerebral Cortex. J. G. Dusser de Barenne, New Haven, Conn.—p. 573.
Review of Recent Studies on Epidemiology of Poliomyelitis in the United States. J. R. Paul, New Haven, Conn.—p. 577.

Yeastlike Fungi of the Human Vagina.—Weinstein and Wickerham estimated the incidence of the yeastlike fungi in the vaginal secretions of 375 women who were normal or pregnant or had some disease of the female genitalia. In addition to a study of the incidence of the yeastlike organisms, cultural determinations of the remainder of the bacterial flora of the vagina were made in each case, so that the complete bacteriologic picture was obtained. It was found that 23.3 per cent of the pregnant and 7.3 per cent of nonpregnant women harbored yeastlike organisms; that is, 64 per cent of the nonpregnant group and 56 per cent of the pregnant showed signs of infection of the vagina by these organisms. The absence of disease of the vagina when yeastlike fungi are present is not necessarily an indication of the nonpathogenicity of the organism but may indicate a resistance on the part of the host. There seems to be strong evidence for the existence of a carrier state with the yeastlike fungi. Monilia albicans was isolated thirty-five times, Torula nine, Saccharomyces four, Monilia parapsilosis twice and Mycoderma once. The identity of these organisms was established on the basis of cultural and fermentation reactions. Studies of the vaginal flora in cases in which yeastlike fungi were present revealed that the Döderlein bacillus can be recovered with great frequency, thus casting doubt on the inference that this organism is an indicator of vaginal health. Staphylococcus aureus (seven) and albus (thirty-three), hemolytic (eight) and nonhemolytic (eighteen) streptococci and Escherichia coli (four) were also recovered.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2: 1-52 (July 2) 1938

*Treatment of Apoplexy by Infiltration of Stellate Ganglion with Novocain. W. A. Mackey and L. D. W. Scott.—p. 1.
Common Foot Ailments. W. S. Creer.—p. 5.
Tetanus Bacillus Recovered from the Scar Ten Years After an Attack of Postoperative Tetanus. V. Bonney, C. Box and J. MacLennan.—p. 10.
Rising Incidence of Psychosomatic Illness. J. L. Halliday.—p. 11.
*Seasonal Incidence of Rheumatic Fever in This Country. A. B. Rowlands.—p. 15.

Infiltration of Stellate Ganglion for Apoplexy.—Mackey and Scott carried out infiltration of the region of the stellate ganglion on nineteen cases of apoplexy; a definite clinical improvement followed nine of these injections. Only in one case—the youngest patient of the series—was the improvement dramatic, and in this instance the immediate beneficial effect of the treatment cannot be doubted. In the other cases the degree of improvement was relatively slight. In one instance the injection was followed by respiratory failure, apparently produced by the solution being accidentally introduced into a vein. The results obtained do not justify the adoption of anesthesia of the stellate ganglion as a routine method of treatment in apoplexy, but further study is necessary before the method can be rejected as of negligible value. The use of the method in cases of severe cerebral hemorrhage in patients of middle age and older will serve only to bring it into disrepute. Cases of cerebral thrombosis may show some improvement of the clinical condition following anesthesia of the stellate ganglion; the degree of such improvement will be partly dependent on how much arterial sclerosis is present. The ideal case would seem to be one of cerebral embolism, especially in the young. The treatment should be given as soon after the onset of the apoplexy as possible. Only a negligible degree of improvement can be expected if the illness has lasted longer than twenty-four hours before treatment is instituted.

Seasonal Incidence of Rheumatic Fever.—Rowlands shows by a graph the onset of symptoms in nearly 1,500 first attacks of rheumatic fever (St. Bartholomew's Hospital, from 1882 to 1904), from the study of which there can be no doubt that in England there is a significant correlation between the seasonal variations of rheumatic fever and the rates of change of temperature and relative humidity. There are two well established associations between climate and the incidence of rheumatic fever: 1. Newsholme (1935) has clearly demonstrated that the incidence of rheumatic fever is highest in hot dry years. 2. Damp cold has been implicated by numerous workers (Poynton and Schlesinger, 1937). At first glance these associations appear to be mutually antagonistic. Fortunately this paradox is apparent rather than real. The maximal seasonal incidence of rheumatic fever does not occur in the hottest and driest months; neither does it occur in the damp cold of winter. It is to be found between the two, when the hot dry conditions of summer are changing most rapidly to the damp cold of winter. While hot dry conditions predispose to the onset of rheumatic fever, it is the rate of change to damp cold which acts as the precipitating climatic factor.

Glasgow Medical Journal

12: 1-52 (July) 1938

Sulfanilamide in Treatment of Gonorrhea, with Special Reference to a Review of 100 Early Acute Cases. J. G. McGregor-Robertson.—p. 1.
*Para-Aminobenzene Sulfonamide in Treatment of Pyelitis of Pregnancy. A. Barr.—p. 18.

Sulfanilamide in Pyelitis of Pregnancy.—Barr treated sixty-four cases of pyelitis of pregnancy with sulfanilamide. Simple cases can be cured in from four to five days with sulfanilamide. Renal and toxic pyelitis requires a larger dosage of the drug and a longer time (fourteen days) to sterilize the urine. The treatment is more quickly effective than any other standard line of treatment for pyelitis in pregnancy, and now it should seldom be necessary to resort to ureteral drainage or termination of pregnancy in these cases. The immediate improvement in the general appearance of the patient and her obvious feeling of well being shortly after the treatment is begun is in marked contrast to the depression of patients taking large quantities of alkalis. Catheterization of the ureters has been unnecessary in this series even in cases of the gross toxicity. Induction of premature labor was not necessary and all patients with the exception of the two in whom miscarriages occurred went to term. In slight pyelitis from 0.5 to 0.6 Gm. of sulfanilamide three times a day rapidly produced a remission of symptoms—usually within forty-eight hours. In the severe cases a dosage of from 1.8 to 2.4 Gm. a day was required to sterilize the urine in an average of fourteen days. In the toxic cases in which nausea and vomiting were prominent features, oral administration of the drug was impossible and daily injections of prontosil (Winthrop) were given in 10 cc. doses, and in from four to five days administration of the drug by mouth was usually possible. Administration of prontosil did not seem so effective and in from five to seven days, although there was a slow improvement in the general condition of the patients, there was no material change in the bacterial content of the urine. As soon as the administration of sulfanilamide by mouth was begun there was a rapid change in the general condition, and the urine was sterile in an average of fourteen days as in the renal cases, with the same dosage.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

45: 405-596 (June) 1938

Urinary and Fecal Fistulas. N. P. Mahfouz.—p. 405.
*Etiology of Thrombosis and Embolism. D. Dougal.—p. 425.
*Postoperative Exercises as Preventive of Embolism. W. F. Shaw and C. E. B. Rickards.—p. 451.
Postpartum Necrosis of Anterior Pituitary: Pathologic and Clinical Aspects. H. L. Sheehan and R. Murdoch.—p. 456.
Operation for Cure of Congenital Absence of Vagina. A. H. McIndoe and J. B. Banister.—p. 490.
*Treatment of Puerperal Sepsis by Prontosil and Allied Compounds. Doris B. Brown.—p. 495.
Induction of Labor by Puncture of Membranes: Review of 357 Cases. R. A. Tennent.—p. 509.

Etiology of Thrombosis and Embolism.—Dougal contends that tissue trauma and sepsis are the two primary causative factors of thrombosis and embolism and that as they frequently coexist in cases of thrombosis it is difficult to decide which is the more important. Slowing of the circulation is so important a predisposing cause of thrombosis that it is almost a sine qua non. There are certain contributory factors. The main problem in etiology is to find why intravascular clotting is liable to occur after labor or a surgical operation. The author is of the opinion that a subtotal hysterectomy is more liable to be followed by thrombosis than a total hysterectomy, and he believes the reason to be that in the latter operation a small opening is left for drainage at the upper end of the vagina. If there is no drainage a certain amount of blood or tissue juice may be retained and serve either as a source of thrombokinase or other coagulant or as a nidus for the growth of low grade micro-organisms. He believes the second possibility to be the more likely one. The most important secondary factor is venous stasis, and its presence is usually necessary because thrombosis rarely occurs if the blood flows freely. The blood changes are also important but only to the extent that they cause the blood to coagulate more readily or more efficiently. As these changes are fairly constant in puerperal and postoperative cases, it means that these patients are more susceptible than others to the dangers of intravascular clotting. Injury to the wall of the vessel would be a primary factor if it could be shown that postoperative thrombosis has its origin in ligated, clamped or otherwise injured vessels in the course of surgical intervention, but until this has been demonstrated it must be regarded as a secondary factor linked up with trauma to tissue and sepsis.

Postoperative Exercises as Preventive of Embolism.—By comparing the incidence of postoperative embolism (in two institutions, in wards under the care of the same gynecologist, admitting the same type of patient, with the same preoperative and postoperative treatment—except that in only one institution systematic graduated postoperative exercises were given) Shaw and Rickards assess the value of postoperative exercises as a preventive of embolism. In the hospital in which graduated exercises were performed the incidence of fatal pulmonary embolism was 0.06 per cent in 1,635 consecutive operations. In the other hospital, without graduated

exercises, the same gynecologist in the same twelve years performed 3,618 operations with an incidence of fatal pulmonary embolism of 0.304 per cent, a percentage incidence five times as great as in the other group. The exercises carried out were as follows: The convalescent patients lift their arms high over their heads twenty times and then, lying on their backs, lift each leg the same number of times. During the first few days after an operation the patients cannot elevate their limbs so often but, even a day after an operation, the patient can lift her arms a few times while her legs can be drawn up to her body and then fully extended. This necessitates the removal of the pillow which normally supports her legs, and this is probably one of the greatest benefits, as the constant clinging pressure on the back of the thighs must retard the venous circulation.

Treatment of Puerperal Sepsis by Prontosil.—Brown used prontosil (Winthrop) in the treatment of thirty-nine cases of puerperal sepsis due to the hemolytic streptococcus (group A of Lancefield) and in the treatment of thirty-five cases of mastitis and eight cases of Bacillus coli infection of the urinary tract. Of the thirty-nine patients suffering from puerperal sepsis there were twenty-seven with local infection of the uterus, eight with septicemia (two of whom also had general peritonitis) and four cases of general peritonitis alone. Prontosil was administered intramuscularly and by mouth. Prontosil soluble was used in all the cases of puerperal sepsis, but in four mild cases the dosage was not more than 1 Gm. In the first five cases treated the first dose was given intravenously but in the remainder of the cases by intramuscular injection. It was given in the dosage of 20 cc. (0.5 Gm.) two or three times daily, the amount being decreased as the patient improved. There was marked improvement in eleven of the twenty-seven patients with local infection of the uterus after the administration of prontosil; in one patient it had no effect and in one death occurred from agranulocytosis after the sepsis had apparently been controlled. These patients were seriously ill. In the eleven successfully treated cases the average total dosage of prontosil was 42.6 Gm. The fourteen other cases were of mild or moderate severity and recovery would almost certainly have occurred without prontosil. Of the eight patients with proved septicemia six recovered—a mortality of 25 per cent. One of these patients who died was the first to be treated with prontosil and the dosage was inadequate. The second fatal case was admitted four days after a manual removal of the placenta. Of the four patients with general peritonitis not associated with a septicemia, all recovered. Relapses occurred in three of the patients but responded when the drug was readministered. The thirty-five patients with mastitis have been treated by the administration of sulfanilamide, benzyl aminobenzene sulfonamide or sulfonamide-P (sulfanilamide) in the dosage of from 2 to 3 Gm. daily. The average duration of treatment was five days. All were severe cases and a few of the patients were extremely ill. The mastitis resolved completely and patients in whom mastitis developed in the hospital have not had any abscesses of the breast, that is, since prontosil was used for acute mastitis. The author has also used sulfanilamide in the treatment of a number of patients admitted for abscesses of the breast and although most of these have required incision they have all appeared to heal more rapidly than usual.

Lancet, London

1: 1429-1486 (June 25) 1938

*Natural History of Strawberry Nevi. W. A. Lister.—p. 1429.
Intra-Ocular Pressure in Nephrotic Edema and Its Bearing on Nature of Aqueous Humor. J. D. Robertson.—p. 1435.
Effect of Poor Social Conditions in Production of Neuroses. W. L. Neustatter.—p. 1436.
Acute Lymphatic Leukemia in Childhood. F. D. Hart.—p. 1441.
Production of Diabetes in Dogs by Anterior Pituitary Extracts. J. Campbell and C. H. Best.—p. 1444.
*Therapeutic Effect of Vitamin P in Schönlein-Henoch Purpura. T. Jersild.—p. 1445.

Strawberry Nevi.—From a review of the literature and study of seventy-seven cases (ninety-three nevi) of nevi it appears to Lister that strawberry nevi of infants have a natural history entirely different from that of any other type. The essential point of distinction is that they grow more or less rapidly during the first few months after their appearance. This never continues for more than a year, and commonly it ceases between the sixth and eighth months. Thereafter retrogression sets in. Usually all trace of color has been obliterated by the fifth year, if not earlier, and only the most prominent nevi require more time for the final absorption of the redundant skin. This is the explanation of the uniformly good results recorded by surgeons, whatever the method. Those nevi which develop into large vascular tumors in adults have an entirely different early history. The treatment of strawberry nevi must be based on the knowledge of their invariable tendency to spontaneous retrogression. If the nevus cannot be quickly and safely obliterated, the mother should be reassured that however distressing the disfigurement may now appear it will inevitably fade. The object in advocating expectant treatment is to ensure that ultimately no unsightly or disabling scar will be left. There is more cause for anxiety if a nevus shows no active growth in infancy, for it is then unlikely to retrogress of its own accord.

Vitamin P in Schönlein-Henoch Purpura.—Jersild cites a case of Schönlein-Henoch purpura in which all the characteristic symptoms were promptly influenced by treatment with vitamin P. During the past eight years the patient presented several of the characteristic features of Schönlein-Henoch purpura (vomiting, colic, constipation, occasional blood-stained discharges, purpura, urticaria, transient edema, pain and swelling of joints, renal colic, albuminuria and hematuria). When the capillary resistance was tested by Göthlin's method the patient showed fifty petechiae, which denotes increased permeability of the capillaries. The same result was obtained by suction. There is generally held to be a direct relationship between low capillary resistance and deficiency of vitamin C. Accordingly the effect of ascorbic acid was tested before treatment with vitamin P was begun, and 300 mg. of ascorbic acid was injected intravenously every day for a week. The results were negative. The capillary resistance remained unchanged and fresh ecchymoses appeared spontaneously. Vitamin P was then given in the form of daily intravenous injections of 50 mg. of citrin. During treatment with citrin the capillary resistance rose and the ecchymoses disappeared. When the injection of citrin was stopped the capillary resistance fell and new ecchymoses appeared. When citrin was again given the capillary resistance increased again and the ecchymoses faded. During treatment with citrin the patient lost all symptoms of Schönlein-Henoch purpura. The symptoms characteristic of Schönlein-Henoch purpura may be explained as being the result of an abnormal capillary resistance, and this theory is supported by the observations of Müller (1922), who found dilated, elongated and twisted capillaries in the skin of cases of Schönlein-Henoch purpura. The effect of vitamin P is to regulate the permeability of capillaries and it was undoubtedly this effect which was responsible for the good progress in the author's patient. Thus it seems that one is justified in assuming that Schönlein-Henoch purpura is caused by deficiency of vitamin P.

Japanese Journal of Obstetrics & Gynecology, Kyoto

21: 179-242 (May) 1938. Partial Index

Experimental Study on Effect of Iodides on Growth and Radiosensitivity of Malignant Tumor: Parts IV, V and VI. H. Ito.—p. 180.
Effect of Metabolism of Carbohydrate on Growth and Radiosensitivity of Malignant Tumors. M. Ôsima.—p. 188.
Menstruation and Blood Groups. H. Ito.—p. 210.
*Our Treatment for Serious Neonatal Jaundice. H. Kawakami and E. Yogo.—p. 218.
Efficacy of Tryptan for Anemia in Obstetrics and Gynecology. H. Kawakami, K. Yamada and S. Morimoto.—p. 227.
Clinical Application of Vitamin B, Especially Vitamin B_1, for Toxemia Gravidarum. H. Yasunami.—p. 239.

Neonatal Jaundice.—Kawakami and Yogo treated three cases of severe neonatal jaundice by inserting a catheter into the stomach of the newborn infant and administering through it a preparation of magnesium sulfate and hydrochloric acid: from 2 to 3 cc. of a mixture of 10 Gm. of magnesium sulfate, 1 cc. of dilute hydrochloric acid and 90 cc. of water with from 20 to 30 cc. of mother's milk. This is done three or four times a day at intervals of several hours. The treatment proved efficacious as in from one to three days the jaundice disappeared, the appetite returned to normal and the temperature fell to normal.

Archives des Maladies de l'App. Digestif, Paris

28: 553-672 (June) 1938

Ligation of Gastroduodenal Artery Associated with Gastric Operations in Treatment of Acute Grave Hemorrhages in Duodenal Ulcer. R. Peycelon and A. Trillat.—p. 553.
*Hereditary Hyperbilirubinemia: Familial Cholemia and Hemolytic Icterus. R. M. Tecon.—p. 567.
Pure Fibroma of Stomach. C. Bonorino Udaondo, E. Finochietto and D. Mosto.—p. 590.
Pharmacodynamic Investigations on Morphology of Cellular Secretions. G. Wallbach.—p. 608.

Hereditary Hyperbilirubinemia.—Tecon believes that it is possible and necessary to differentiate between familial cholemia and hereditary hemolytic icterus. The criteria which he regards as valid are not the clinical symptoms, which may be identical, or the hematologic signs or the biochemical aspects, because the microspherocytosis is not constant and it is observed in related conditions; nor is it either the quality or the degree of bilirubinemia. The only conception which is sufficiently comprehensive to take account of all the facts is the biologic idea of the development of the disease in question in an individual, together with his ancestry and descendents. When studying the families of patients with hemolytic icterus and of those with hereditary cholemia in the light of this criterion, it is difficult for one not to conclude that the two types of disorders are closely related but different in their biologic manifestations. This differentiation seems to correspond to the observed facts. The author stresses the following points: 1. Familial cholemia is an independent disturbance, which is hereditary and congenital and which is transmitted according to the laws of heredity with dominant character; it must be clearly differentiated from hereditary hemolytic icterus; it belongs to the group of familial and hereditary hepatoses. 2. Familial chronic hemolytic icterus is a distinct disease, which is congenital and which is transmitted by both sexes according to the laws of heredity with dominant character; it is distinctly different from familial cholemia. 3. The differential diagnosis is easy in the typical cases, but it is so difficult in the atypical cases that it cannot be established with certainty before the patient has been observed for some time, has been subjected to repeated examinations and has had his family history investigated. Moreover, the diagnosis is reliable only if made by a physician who is thoroughly familiar with both disorders. The prognosis and therapy of the two disorders are so different that great efforts should be made to make a precise differential diagnosis.

Gynécologie et Obstétrique, Paris

37: 425-519 (June) 1938

Genital Crises of Tabes and Syphilitic Myelitis in Women. A. Binet.—p. 425.
Consideration of Twelve Fatal Cases of Pulmonary Abscess Observed After Delivery and After Abortion. P. Trillat and R. Burthiault.—p. 434.
*Cardiac Insufficiency After Delivery. P. Broustet and R. Mahon.—p. 453.
Experimental Investigations on Toxicity of Blood in Uterine Fibroma. C. Daniel and I. Florian.—p. 463.
Luteinic Cysts. B. S. ten Berge.—p. 474.
Death of One Set of Twins in Bivitelline Pregnancy. A. Costa.—p. 482.

Cardiac Insufficiency After Delivery.—Broustet and Mahon point out that the view that delivery marks the end of a dangerous period for cardiac patients is not true of all cases. In a certain number of patients the cardiac insufficiency, which was already manifest during gestation, continues during the puerperal period. There are even women with cardiopathy who passed through pregnancy and delivery without accident and in whom severe circulatory accidents developed during the postpartal period. The author believes that among women with cardiopathy the incidence of postpartum cardiac insufficiency is approximately 16 per cent. Of ten women with mitral cardiopathy who arrive at the end of their gestation, one or two are likely to develop manifestations of cardiac insufficiency after delivery. This cardiac insufficiency takes the form of a progressive asystole or of an acute pulmonary edema. The author thinks that these cardiac insufficiencies are essentially the result of the reentry into the general circulation of the masses of blood that accumulated after delivery in the venous depots of the abdomen. This encumbrance of the circulation in turn elicits a crisis of acute edema in the patients with well compensated mitral cardiopathies, in whom until then the auricle was hypertrophied but not dilated. In others, in whom the auricle was already deficient and the pulmonary circulation overloaded, it produces a progressive augmentation of the pulmonary stasis, which often advances inexorably. The evolution of this form involves great danger, especially if it is accompanied by fever. The immediate and ultimate prognosis of acute edema is much more favorable. The fact that the woman is in the puerperal stage does not alter the classic treatment of these diverse manifestations of cardiac insufficiency.

Presse Médicale, Paris

46: 1065-1080 (July 6) 1938

*Nonpulmonary Form of Hemoptysis: Tracheal Hemorrhages (Hemorrhagic Tracheitis). V. Cordier and P. L. Mounier-Kuhn.—p. 1065.
Postserotherapeutic Radial Paralysis. C. Angelesco, A. N. Popovici and I. Balutza.—p. 1068.

Tracheal Hemorrhages.—Cordier and Mounier-Kuhn reserve the term tracheal hemorrhages for repeated hemoptyses, the tracheal origin of which is verified by endoscopy and in a less distinct manner by indirect tracheostomy. The authors say that the patients may request medical aid at the time of their first hemoptysis or because, although apparently in good health, they have had blood in the sputum for some time. Systematic bronchoscopy and clinical examination may suggest the possibility of a tracheal hemorrhage. The hemoptyses differ; a mouthful of blood may be expelled after a sudden effort, but in the majority of cases the expulsive cough is absent. In this respect the condition differs from tuberculous hemoptysis, in which the expulsive cough is rarely absent. The expectoration without effort (but with retrosternal tingling) impresses and reassures the patient; in drawing the physician's attention to this, he puts him on guard against an overhasty diagnosis of tuberculous hemoptysis. A definite diagnosis should never be made without a tracheoscopy, which may reveal (1) individualized lesions, such as malignant or benign tumors or, in exceptional cases, syphilitic or tuberculous lesions, (2) autochthonous tracheal lesions, which are diffuse, indicating sanguineous dyscrasias (tracheal purpura, angeitis of Osler and so on) and (3) a hemorrhagic tracheitis with fixed topography, probably in relation to a tuberculous adenomediastinitis; these tuberculous lesions are old but the hemorrhagic tracheitis, although it may make careful observation necessary, does not have to be treated like a developing tuberculous process. Besides these cases there exists still another form of tracheal hemorrhage for which no explanation has been found as yet. The author says that treatment is of little avail. Local application of cocaine-epinephrine or of silver nitrate have an ephemeral effect in most cases. Inhalation of antiseptic vapors or similar measures are ineffective. The employment of coagulants is beneficial; if a spirochetosis exists, acetarsone is often efficacious. In angiomatous tumefactions, cauterization gives temporary improvement. However, the diagnosis of the disease is generally more important than is the cure, as was indicated by observations on several patients whose lives had been spoiled by worries about these repeated hemorrhages.

46: 1097-1112 (July 13) 1938

*Action Mechanism of Male Hormones in Hypertrophy of Prostate. C. Champy, Heitz-Boyer and R. Coujard.—p. 1097.
Anginas in Carriers of Diphtheria Bacilli. J. Paraf and P. Boulenger.—p. 1101.
New Cures of Acute Spasmodic Postoperative Ileus by Simple Spinal Anesthesia. T. Asteriadès.—p. 1103.

Male Hormones in Hypertrophy of Prostate.—Champy and his associates point out that a connection between the hypertrophy of the prostate and disturbances in the internal secretion of the testes has been suggested for a long time. They cite authors who observed regression of the prostatic hypertrophy after castration and they also direct attention to the effect of the suppression of the external secretion by means of ligation of the deferent ducts. On the other hand, it has been suggested that the internal testicular secretion be stimulated rather than the external secretion suppressed. The authors show that it is not illogical that the one as well as the other method will produce results. They cite animal experiments as well as clinical observations and explain the action of the sex hormones on the

prostate and the action of Steinach's operation. From the practical point of view they give preference to the treatment with purified testicular lipoids, because these show themselves more active on the perivascular edema of the prostate than their equivalent of testosterone. Moreover, the purified testicular lipoids are easily administered by the digestive tract. This mode of administration permits the distribution of the doses. The latter factor appears essential to the authors in that the hormones are not entirely harmless. In order to produce a reaction in the genital glands, it is not necessary to give large quantities of hormone every day. The injection produces "peaks" in the hormone content of the blood, which may be useful at the time of an attack, but the authors regard it as imprudent to prolong this condition. The treatment must be continuous, as in the case of insulin therapy, but in strictly sufficient doses. Endocrine therapy can be useful also as an adjuvant to the endoscopic resection of the hypertrophied prostate, in that it will make the effects of this surgical treatment more lasting. The authors say that one of them recommended the combination of surgical and endocrine treatment as early as 1930. As the endoscopic operation cannot entirely destroy the adenoma, they think that it is advisable to try to arrest the growth of the adenoma and to restore to the smooth muscle the extensibility it has during youth.

Monatsschrift f. Geburtshülfe u. Gynäkologie, Basel

108: 57-124 (June) 1938

Difficulties in Breast Feeding and How to Overcome Them. R. T. von Jaschke.—p. 57.
*Clinical and Experimental Observations in Vitamin C Tolerance Tests During Menstrual Cycle. H. Winkler and W. Seebach.—p. 67.
Sterilization by Knotting of Uterine Tubes. H. Gänszbauer.—p. 83.
Action Mechanism of Female Sex Hormones. F. Kovács.—p. 93.

Vitamin C Tolerance During Menstrual Cycle.—In the first part of this paper Winkler and Seebach evaluate the different methods that have been recommended for the determination of ascorbic acid. Further, they studied the curve of elimination in case of oral and of parenteral administration. They found that in case of intravenous administration the maximum of the elimination is reached in from sixty to ninety minutes after the injection; the curve remains at this level for about one hour and after that decreases suddenly. In case of intramuscular injection, the maximum is reached less suddenly; the curve has two peaks (after one and a half and three and a half hours). This curve indicates that the depot produced by intramuscular injection is slowly evacuated. In case of oral administration, the curve rises in a straight line until the maximum is reached in about three and a half hours, but one hour later it already has declined again. In the second part of their report, the authors discuss ascorbic acid tolerance tests during the menstrual cycle. In tolerance tests on twelve women they were unable to find a relation between the menstrual cycle and the ascorbic acid elimination in the urine. In eight of the women examined, disturbances in the general condition resulted, such as headaches, lack of appetite, vertigo, fatigue, depression and reduced capacity of association. The headaches usually appeared two or three hours after oral administration. The fact that the disturbances appear on the second or fourth day of the tolerance test, that is, at a time when the organism is not yet saturated with the vitamin, indicates that hypervitaminosis cannot be the cause of the disturbances. The freedom from disorders in case of the parenteral intake of the vitamin and their severity in case of oral administration suggest that the mode of absorption is an important factor in their development. The authors suggest that the administration of sodium bicarbonate will help in preventing the disorders without interfering with the absorption of the vitamin.

Archivo Italiano di Chirurgia, Bologna

48: 697-792 (May) 1938

*Appendicular Mesenteriolitis. E. Beluffi.—p. 697.
Vesical Bilharziasis. A. Cassuto.—p. 745.
Chyle Angiectasia and Cystic Lympho-Angio-Endothelioma of Mesentery. E. Fiorini.—p. 758.

Appendicular Mesenteriolitis.—Beluffi made microscopic studies of 245 appendixes and their mesenteries which were surgically removed for various forms of chronic or acute appendicitis. He concludes that the appendicular mesentery shows microscopic lesions which vary with the form of appendicitis and are proportional to the intensity of the disease. In acute appendicitis the mesentery shows edema, exudation, cellular infiltration, lymphangitis, rapid mobilization of reticulo-endothelial cells and perivascular infiltration. In grave cases, alterations of the local circulation take place and may be complicated by venous thrombosis and, in rare cases, by suppurative thrombophlebitis or liver abscess. After regression of acute appendicitis the appendicular mesentery shows structural changes such as retraction, formation of adhesions, thickness of the connective tissue and of the vascular walls and also the presence of lymphatic infiltration. The structural changes of the mesentery after acute appendicitis are permanent. Their presence allows a retrospective diagnosis of acute appendicitis. The structural changes of the mesentery induce mechanical and functional disorders of the appendix by which secretory stasis and the development of further attacks of acute appendicitis are stimulated. It seems possible that the infection may be transmitted through the mesentery to distant abdominal viscera even after appendectomy, which fact shows the advisability of performing an ample removal of mesentery during appendectomy followed by peritoneization of the cut surfaces of the structure.

Cuore e Circolazione, Rome

22: 289-340 (June) 1938

Chronic Circulatory Insufficiency in Right Pleuritis with External Mediastinopericarditis. G. Pelà.—p. 289.
*Ketone Bodies in Blood and in Urine in Decompensated Heart Diseases. L. Capani.—p. 304.
Malformation of Heart and Congenital Complete Atrioventricular Dissociation: Case. A. Calò.—p. 323.

Ketone Bodies in Heart Diseases.—Capani studied the behavior of the ketone bodies in the blood and urine of fourteen patients suffering from heart diseases in different phases of decompensation. He found that ketonemia is almost normal in decompensated heart diseases without edema and increased in the presence of edema. Ketonemia parallels the intensity of edema and diminishes with improvement of the circulatory conditions. The highest levels of ketonemia are observed in the blood of patients who are in the preterminal phase of decompensated heart disease with anasarca. There is no relation between ketosuria and ketonemia. Ketosis in decompensated heart diseases with edema depends on the diminished velocity of the circulation, which results in a diminished ketolysis at the tissues and disorders in the interchange between the blood and the interstitial fluids with consequent accumulation of ketone in both fluids.

22: 341-396 (July) 1938

Electrocardiography in Acute Attack of Angina Pectoris. E. Secondari.—p. 341.
*Cardarelli-Katzenstein Test for Function of Heart: Behavior of Peripheral Venous Pressure. G. Chiorazzo and D. Perini.—p. 354.
Variations of Reactive Hyperemia and Behavior of Temperature After Occlusion of Circulation in Some Vascular Diseases. G. Personeni.—p. 368.

Venous Pressure During Occlusion of Femoral Artery.—Chiorazzo and Perini induced occlusion of the femoral artery in thirty cases by means of the application of an elastic bandage at the thigh (Cardarelli-Katzenstein test). They found that the test in normal persons induces transient tachycardia, which is followed by bradycardia, increased systolic pressure in the arteries and diminution of the venous pressure. This circulatory phenomenon disappears immediately after removal of the elastic occluding bandage. The greatest arterial pressure may or may not be increased in the course of the test in persons who do not have heart disease but a hypotonic heart. In all cases, however, the venous pressure diminishes during the test. In heart diseases with actual or latent decompensation the test induces tachycardia, lowering of the greatest arterial pressure and increase of the venous pressure. In actual or latent insufficiency of the left side of the heart the arterial and venous pressure diminishes during the test. Patients who are suffering from heart disease and react as do normal persons during the test are considered as having lasting compensation. According to the authors the test shows myocardial insufficiency early in the evolution of the disease, at a time at which the clinical symptoms of decompensation have not yet appeared. Several types of heart insufficiency can be differentiated by the behavior of the venous pressure in the course of the test.

Policlinico, Rome

45: 297-344 (July 15) 1938. Surgical Section

Process of Reparation of Fractures Following Functional Exclusion of Kidney: Behavior of Calcemia in These Pathologic Conditions. F. De Victoriis-Medori.—p. 297.

Torsion of Spermatic Cord in Inguinal Retention of Testicle: Clinical and Anatomic Study. L. Giornelli.—p. 320.

*Elimination of Urea, Phenolsulfonphthalein and Indigo Carmine in Separated Urine in Eleven Cases of Renal Blastomatosis. D. Torre.—p. 332.

Renal Cancer.—Torre observed the elimination of urea, indigo carmine and phenolsulfonphthalein in the separated urine of both kidneys of eleven patients suffering from unilateral renal cancer. He found that the urea was eliminated at the same speed and concentration by the normal as by the cancerous kidney in nine cases, whereas it was delayed and insufficient in two. The elimination of indigo carmine was also the same for the two kidneys in nine cases whereas it was diminished in two. The phenolsulfonphthalein test gave the same results for the two kidneys in seven cases. In four the elimination of phenolsulfonphthalein by the cancerous kidney was insufficient and the normal kidney was in vicarious hyperfunction. The microscopic study of the renal parenchyma showed that the portion which was not infiltrated by cancer was normal in nine cases. It was the seat of sclerosis in one case and of suppuration in another case. In both cases the tests of elimination of urea and color substances gave results showing deficiency. The author concludes that the results of chromoscopy and of the tests of elimination of urea and phenolsulfonphthalein may be erroneous, showing normal function of the cancerous kidney even in advanced phases of the condition if a certain part of the renal parenchyma is not involved by the tumor. The results of the tests show insufficiency of the structure if the renal parenchyma is the seat of lesions other than involvement by the tumor. The false results of the tests in the presence of unilateral renal cancer depend on the preservation of the renal parenchyma and on a dysfunction of the metabolism of urea which takes place in the course of unilateral renal cancer, owing to a reflex hypofunctioning action of the cancerous kidney on the normal kidney.

Beiträge zur klinischen Chirurgie, Berlin

167: 513-674 (June 1) 1938. Partial Index

Growth Disturbance of Ollier's Type (Dyschondroplasia). W. Stark.—p. 513.

*Lipoidosis of Gallbladder. T. Ahlin.—p. 555.

Treatment of Central Dislocation of the Hip. B. Karitzky.—p. 577.

Acute Osteomyelitis. W. Inthorn.—p. 595.

Present Status of Cholecystostomy and Its Results in Frankfort Clinic. H. Geissendörfer.—p. 609.

*Studies on Origin and Significance of Strawberry Gallbladder. E. Fenster.—p. 641.

Lipoidosis of Gallbladder.—Ahlin states that lipoidosis of the gallbladder is a fairly frequent observation in the pathologic section of St. Erik's hospital, Stockholm, and that it is found in various diseases. The sex distribution is about equal. There is an increase in the frequency between the ages of 40 and 50 years for women, whereas in man the incidence is about equal for the various ages. The gallbladder lipoidosis is in no way related to inflammatory alterations in the gallbladder wall and does not lead per se to serious disturbances. General disturbances of lipoid metabolism play a part in the production of gallbladder lipoidosis. The frequent occurrence of this condition in obese persons speaks for this. Local conditions which, however, are as yet not understood may furnish the explanation for the occurrence of the condition by retention of lipoids in the mucosa. With the exception of pure cholesterol stones, the concurrence of stones and lipoidosis of the gallbladder is rare. For this reason the author considers it improbable that lipoidosis must precede stone formation and that there is a direct relationship between the two. However, it would be impossible to deny the existence of common etiologic factors for the two processes. Lipoidosis of the gallbladder is apparently a reversible process capable of complete restitution to the normal. The author's studies do not support Bernhard's conclusion that patients with gallbladder lipoidosis are more predisposed to cancer than other patients.

Strawberry Gallbladder.—The concept "strawberry gallbladder" as an independent disease entity, according to Fenster, and the contradictory interpretation of it as an accompanying lesion in the presence of other gallbladder and liver diseases is due to the fact that the pathologists recognize two varieties of strawberry gallbladder; namely, the one characterized by an ordinary network and the other characterized by the formation of polyps. There is considerable unanimity as to the the clinical picture. The author stresses the frequency of pericholecystic adhesions and enlargement of the lymph nodes of the cystic duct as one of the causes of the slowing of the lymph current in the gallbladder area and its role in the so-called serous inflammation. On the basis of his own experiments, the author favors the idea of absorption of cholesterol rather than of secretion, while at the same time rejecting inflammation as the only cause of development of the strawberry gallbladder. The role of certain mechanical conditions such as gallbladder stasis and dyskinesia are admitted. Fenster considers the cholesterol esters found in the bile of such gallbladders as a product of secretion of the bile and feels that its occurrence, as well as that of the quinine-resisting liver lipase in the blood, is a proof of the existence of damage to the liver parenchyma. The presence of larger deposits up to the formation of small polyps and the frequent occurrence of mulberry stones point to the relationship between strawberry gallbladder and gallstone formation. The frequent involvement of the pancreas is regarded in the same light as the parenchymatous lesions of the liver as a proof that strawberry gallbladder is not a harmless condition of local significance but an independent disease entity. The author stresses diagnostic difficulties, particularly in differentiating the strawberry gallbladder from dyskinesia. He advocates operative removal of the strawberry gallbladder combined in certain cases with dilation of the sphincter of Oddi. He regards the operative intervention as causative therapy in that it frees the patient from pain, removes the dyskinesia as well as a disease link in the gallbladder-pancreas-spleen system, as well as prophylaxis against gallstone formation.

168: 1-176 (July 13) 1938. Partial Index

*Experimental and Clinical Studies on Gastric Secretion After Operative Removal or Functional Loss of Gallbladder. F. Bernhard and T. Eck.—p 1.

Blood Transfusions and Care of Donors in Surgical Clinic of the University of Göttingen. H. Wille-Baumkauff.—p. 23.

Treatment of Damage to the Ureter Occurring in Course of Pelvic Operations. A. Kalo.—p. 33.

Value of Roentgenologic Studies of Layers of the Body (Tomography) in Surgery. G. Arndt.—p. 39.

Role of Thyroid in Clinical Course of Rickets. W. Haase.—p. 64.

Gastric Secretion After Cholecystectomy.—Bernhard and Eck state that, in 160 patients who had had a previous cholecystectomy, the gastric symptoms most frequently associated with gallbladder disease were in some cases relieved, while in some the operation had initiated these gastric disturbances and in others had no influence on them of any kind. The authors prepared a Pavlov pouch on five dogs, determined its secretory status and in a subsequent operation removed the gallbladder and then made further determinations of the gastric secretion. They noted a diminution in acid secretion in three of the dogs, while in two there was no alteration. They did note, however, an alteration in the manner of the secretion of the gastric juice. The pepsin content of the juice was regularly lowered, and the peak of the pepsin and the acidity was arrived at after a considerably delayed period. They concluded from their animal experiments that the removal of the gallbladder alone did not account for the high degree of subacidity and anacidity in patients suffering from gallstone disease. They have further shown that the pancreas and the liver as well as the gastritis and injuries to the vagus have a part in these alterations. It appeared that the beneficial influence on gastric secretion, as the result of the removal of the gallbladder, was limited to a few clinical forms of gallbladder disease. The authors studied the effect of cholecystectomy, which had been performed not less than fifteen years previously, on the gastric complaints and tolerance to fat of 175 patients. They noted that cholecystectomy performed for catarrhal cholecystitis without stones or for chronic cholecystitis with stones did not influence gastric complaints particularly favorably. The results, on the other hand, in acute and subacute cholecystitis were strikingly good. The fat tolerance was frequently aggravated through a cholecystectomy in catarrhal cholecystitis but markedly improved in the other two forms. The statements of the earlier authors as to

the frequency of subacidity and anacidity after cholecystectomy are not accurate for the reason that the height of acid secretion in the stomach of men after the removal of the gallbladder is not infrequently delayed so that the ordinary evacuation of the stomach contents gives erroneously low values. The authors stress the advisability of administering hydrochloric acid and pepsin before meals to patients with subacidity or anacidity.

Deutsche Ztschr. f. d. ges. gerichtl. Medizin, Berlin

30: 1-58 (July 6) 1938. Partial Index

Histologic Examination of Mark Made by Hanging. H. Roer and H. Koopmann.—p. 1.

Question of Combined Air Embolism of Small and Systemic Circulation After Attempted Abortion. F. Hausbrandt.—p. 19.

Postmortem Preservation of Immunity Changes in Blood and Tissues: Limits of Diagnostic Utilization. C. M. Cattabeni.—p. 33.

Automatic Pipet for Determination of Alcohol Content of Blood According to Widmark. G. Weyrich.—p. 43.

*Neuritis Caused by Prophylactic Vaccination Against Tetanus. K. Mészáros.—p. 45.

Determination of Paternity by Means of Blood Group and Civil Law. H. Schneickert.—p. 50.

Neuritis Caused by Prophylactic Tetanus Serum.—Mészáros says that the neuritis caused by vaccination against tetanus is comparatively rare. However, a knowledge that it may occur is important in decisions on accident compensation, since the neuritis caused by the tetanus serum may persist after the cure of the accidental injury. The author reviews the literature on this problem and then describes a case of his own observation. The patient developed an urticaria-like exanthem eleven days after the prophylactic tetanus vaccination and then neuralgic pains in the right arm and weakness in the right deltoid muscle, in the anterior serratus, in the latissimus dorsi and in the infraspinatus. On the basis of the connection in time and of the typical localization in the region of the fifth and sixth cervical roots, the neuritic symptoms must be regarded as sequels of the protective vaccination against tetanus, the more so since no other cause of the paralysis was demonstrable. The course may be designated as favorable, since the condition of the patient improved in nine months to such an extent that the patient could take up his work again; but even after two years there still remained a slight impairment. The assertion of some physicians that the damage to the nerves could not have been caused by the tetanus injection, since it had been made under the skin of the chest, that is, at a site distant from the impaired nerve, is refuted by the fact that the tetanus serum with its antitoxin content does not exert its action at the site of injection but after resorption attacks distant nerves. This is proved also by three other cases cited by the author. He concludes that these rare complications offer no argument against the prophylactic use of tetanus serum. Complete cure is usually obtained in about two years.

Zeitschrift für Kinderheilkunde, Berlin

60: 1-76 (June 20) 1938

Casuistic Contribution to Schaumann's "Benign Granulomatosis." O. Naumann.—p. 1.

Outcome of Convulsions During Early Childhood and Their Modification by Roentgen Rays. E. Wittermann.—p. 9.

Development of Wrist Joint During First Year of Life and Rickets. E. Graser.—p. 30.

*Vitamin E: Its Action on Lactation of Mothers and Growth of Their Nurslings. G. Gaedke and C. Bennholdt-Thomsen.—p. 52.

Investigations on Phosphorus Ester in Human, Cow's and Goat's Milk. G. De Toni and G. Graf.—p. 74.

Vitamin E and Lactation.—Gaedke and Bennholdt-Thomsen say that it is generally assumed that vitamin E, the antisterility factor, has a favorable effect on lactation. However, no objective scientific proofs have been furnished as yet that vitamin E does stimulate lactation. For this reason the authors decided to study the action of additions of vitamin E to the normal diet, of the lactating action of wetnurses and on the growth of their nurslings. Of six wetnurses, two served as controls and were given only inactive substances. It was found that the quantity as well as the fat content of the milk remained uninfluenced by the addition of vitamin E to the normal diet. The infants being nursed by the wetnurses receiving the addition of vitamin E showed no essential difference in their increase in weight from the other two nurslings. The rates of growth in length likewise showed no deviations. All fluctuations were within the limits of the physiologic norm. Neither the wetnurses nor their children showed differences in their subjective conditions which could be ascribed to vitamin E. Moreover, the hemoglobin content of the blood of mothers and children remained uninfluenced by the fertility vitamin. The authors further describe animal experiments on vitamin E. They found that four of a litter of eight young rabbits which were given vitamin E in oil once a week showed retardation in their growth in comparison to the four other animals, which were given the same quantity of inactive olive oil. Three of the four animals which had undergone treatment with vitamin E died later as the result of the administration of massive doses of vitamin E, whereas only one of the four controls died. Studies on animals of another litter indicated that these unfavorable effects of vitamin E on rabbits were not the result of a hypervitaminosis but rather of some substance in the wheat germ oil.

Finska Läkaresällskapets Handlingar, Helsingfors

80: 919-984 (Dec.) 1937

*Subconjunctival Epithelial Cyst and Trachoma: Case. S. Werner.—p. 919.

Lactoflavin (Vitamin B_2) in Retina in Different Conditions of Adaptation. M. Zewi.—p. 923.

*Foramen Ovale Cordis Apertum and Its Role in So-Called Paradoxical Embolism. L. Löfgren.—p. 937.

Subconjunctival Epithelial Cyst and Trachoma.—Werner describes an epithelial cyst in the conjunctiva which was about 1.5 cm. long and 0.3 cm. thick. Nine years earlier trachomatous granulations in the same eye had been treated by expression. In the connective tissue of the lids, numerous trachoma granulations were still seen. He ascribes the tumor to epithelial proliferation or to fold formation in the connective tissue, probably due to the inflammatory trachomatous process.

Role of Foramen Ovale in Paradoxical Embolism.—Löfgren says that in 785 necropsies (in 615 males and 170 females, including no children under the age of 10) foramen ovale cordis apertum was found in 120 cases, or 15.3 per cent. It varies considerably in size and form, the usual diameter being from 2 to 5 mm., while the largest opening is passable to a finger. Unlike a number of other anomalies in the heart, it does not affect physical development or length of life. According to Frey, thrombi in cases in which there is open foramen ovale most often pass from the right auricle to the right ventricle. However, when there is a pulmonary embolus simultaneously with open foramen ovale, possible thrombi in the right auricle which are of the size to pass the foramen ovale are, because of the changed conditions of pressure, passed by way of the left auricle and ventricle into the arterial circulation, where small, otherwise harmless, thrombi may cause death. In cases with the open foramen ovale and simultaneous pulmonary embolus, thrombi as a rule pass through the foramen. Thrombi may often remain in the open foramen, and crossed air and fat emboli may occur in cases with open foramen ovale.

Ugeskrift for Læger, Copenhagen

100: 719-748 (June 30) 1938

Elimination of Androgen in Urine During Treatment of Adiposogenital Dystrophy with Gonadotropic Hormone. K. Sand and P. Plum.—p. 719.

Application of Chemotherapeutics of Sulfanilamide Group in Treatment of Gonorrhea: Preliminary Report. A. Kissmeyer.—p. 724.

*Treatment of Gonorrhea with Sulfanilamide (Streptamide Leo). A. Kristjansen and O. Kaalund-Jørgensen.—p. 730.

Tuberculous Meningitis During Pregnancy: Case. H. Harpøth.—p. 739.

After-Examination of Lupus Patients in Jylland. S. Lomholt.—p. 740.

Treatment of Gonorrhea with Sulfanilamide.—Kristjansen and Kaalund-Jørgensen treated 118 patients with sulfanilamide from December 1937 to May 1938. The by-effects were grave in only one case (hepatitis). The treatment was effective in forty-one (82 per cent) of the fifty women, none of whom were observed for less than six weeks. Three cases are listed as possible "late recurrences." The results were good in twenty-nine (85 per cent) of the thirty-four men with complications. Good results also followed in one of the nine men with infections of less than three weeks' duration, and in thirteen of the nineteen with infections of more than three weeks' duration. The author found that patients resistant to sulfanilamide were later easily affected by other treatment. Recurrence in men after treatment with sulfanilamide was within fourteen days after ending treatment; late recurrences in men were not seen.